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

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# An outbreak of community-associated methicillin-resistant *Staphylococcus aureus* infection in a boarding school in Hong Kong (China)

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**Background:** In November 2012, an outbreak of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) skin and soft tissue infections affecting students at a boarding school in Hong Kong (China) was detected.

**Methods:** A case was defined as any student or staff notified with MRSA infection from 25 October 2012 to 5 July 2013 with the clinical isolate being of staphylococcal cassette chromosome mec type IV or V and positive for Panton-Valentine leukocidin gene. We conducted field investigations, advised on control measures and enhanced surveillance for skin and soft tissue infections at the school. Decolonization therapies were offered to all cases and contacts, and carrier screening was conducted.

**Results:** There were five cases; two (40%) were hospitalized and three (60%) required surgical treatments. Initial screening comprised 240 students and 81 staff members. Overall, four cases (80%) plus eight other students (3.3%) were carriers, with eight of 12 (66.7%) from the same dormitory. All staff members screened negative. After intensified control measures, the number of students screened positive for CA-MRSA decreased from nine to one with no more cases identified in the school.

**Conclusion:** Identification of carriers, decolonization therapy, monitoring of cases and contacts and strengthening of environmental and personal hygiene were control measures that helped contain this CA-MRSA outbreak in a boarding school in Hong Kong (China).

ommunity-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) outbreaks in schools usually affect members of sports teams who come into bodily contact with one another. Considered as more virulent and transmissible than traditional MRSA strains,<sup>1</sup> CA-MRSA may lead to outbreaks associated with severe morbidities and hospitalizations in otherwise healthy young adults or teenagers.<sup>2</sup>

CA-MRSA has been a statutory notifiable disease in Hong Kong (China) since 2007. Medical practitioners are required to report any patient with confirmed MRSA infection fulfilling the surveillance definition and to submit the culture isolate to a government public health laboratory for CA-MRSA confirmatory testing. The disease is rapidly emerging as annual numbers surged from 173 in 2007 to 813 in 2012. Most cases are sporadic skin and soft-tissue infections (SSTIs) with occasional clusters occurring in domestic settings.<sup>3</sup>

School X is a boys' boarding school in Hong Kong (China). In addition to academic teachings, the campus has a marine activities centre, and students spend a significant amount of school time in water sports or training. There are about 250 students living in six dormitories (about 40 students in each one) with plenty of mixing activities among students during training and daily activities.

In October and November 2012, the Centre for Health Protection received three reports of CA-MRSA SSTIs among students from School X, which had no previous reports of CA-MRSA SSTI. Therefore, the case-based investigations were expanded to an

Submitted: 10 October 2013; Published: 17 January 2014

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doi: 10.5365/wpsar.2013.4.4.005

outbreak investigation to determine the extent of the outbreak and to identify possible source(s) of infection. In this report, we present the outbreak investigation, including the implementation and outcome of control strategies.

# **METHODS**

### **Case definitions**

A case was defined as any student or staff member of School X who was notified with SSTIs (e.g. boil, abscess and pustule) or other infections (e.g. pneumonia, sepsis) from 25 October 2012 to 5 July 2013, with MRSA isolated from any clinical specimen with the isolate being of staphylococcal cassette chromosome *mec* (SCC*mec*) type IV or V and positive for Panton-Valentine leukocidin (PVL) gene.

A carrier was any student or staff member of School X, without a clinical infection, who had MRSA isolated from any screening specimen collected from 25 October 2012 to 5 July 2013 with the isolate being of SCCmec type IV or V and positive for PVL gene. Cases were considered carriers if they had a positive screening result after their initial diagnosis.

## Case and carrier finding

Screening of students (after obtaining consent from parents/guardians) and staff from School X was

conducted from 5 November 2012 to 22 March 2013. Initially limited to close contacts of the first notified case (e.g. students in same dormitory, contact-sport team members), screening was extended to all students and staff when the second case was notified (i.e. outbreak established) in November. Attack rates (AR%) by dormitory were calculated by dividing the number of cases and carriers identified by the total number of students in the dormitory, assuming the total number remaining constant during the investigation period.

#### Screening phases and decolonization

Decolonization therapies were offered to cases and screened contacts regardless of carrier status. The five-day regimen comprised daily application of a 4% chlorhexidine gluconate solution as liquid soap and shampoo together with thrice daily application of a topical 2% mupirocin cream to nostrils bilaterally.

Results of decolonization therapies were assessed by post-decolonization screening: Phase 1 aimed to screen all students and staff once, and this occurred over four occasions from 5 November 2012 to 28 January 2013; Phase 2 occurred between 29 January and 12 March 2013, when post-decolonization screening of carriers and cases was completed; Phase 3 occurred from 13 to 22 March 2013, when all cases and Dorm A students were targeted; and Phase 4 occurred between 23 March and 5 July 2013, when the carriers identified in Phase 3 were re-screened (**Table 1**).

# Table 1. Summary of CA-MRSA outbreak in School X by screening phase, Hong Kong (China), November 2012 to July 2013

| Phase                  | Phase 1 (control)   | Phase 2<br>(control and follow-up)                      | Phase 3<br>(intensify control)                               | Phase 4<br>(surveillance and follow-up) |
|------------------------|---|---|--|---|
| Period                 | 5 November 2012 to<br>28 January 2013   | 29 January 2013 to<br>12 March 2013                     | 13 to 22 March 2013  | 23 March 2013 to<br>5 July 2013         |
| Summary                | 4 rounds covering<br>236 students and 81 staff;<br>included screening and<br>decolonization | Post-colonization<br>screening of carriers and<br>cases | Targeted re-screening<br>of all cases and Dorm A<br>students | Follow-up screening of<br>carriers      |
| Number that            | 9   | 4   | 4  | 1                                       |
| screened<br>positive*  | (Cases 1, 2)<br>(Carriers 1–7)  | (Cases 3,4)<br>(Carriers 1, 2)                          | (Cases 1, 4)<br>(Carriers 1, 8)                              | (Case 4)                                |
| Number of new carriers | 7<br>(Carriers 1–7)   | 2<br>(Cases 3,4)  | 1<br>(Carrier 8)   | 0                                       |

\* Number screened positive in each phase included (a) those who remained in carrier status despite decolonization therapy offered in previous phase and (b) both cases and non-case carriers.

# Laboratory testing

Nasal, axillary and perineal swabs were collected during the screenings and were sent to the Public Health Laboratory Service Branch for culture, PVL gene polymerase chain reaction (PCR), SCC*mec* typing, molecular *spa*-typing as well as antibiotic susceptibility tests.

# **Field visits**

Field investigations were conducted by the investigation team, infection-control nurses and a microbiologist. Mixing opportunities in school premises, hygiene facilities and practices were reviewed in each field visit.

# Surveillance

From 25 March 2013, School X was requested to submit weekly reports of any skin lesions identified among students and staff to allow for early detection of potential new cases, timely referral for diagnosis, laboratory investigation and treatment.

# RESULTS

# Cases

Five cases were identified, aged between 13 and 16 years (median 15 years). Four lived in Dorm A (4/41, AR = 9.8%) and one in Dorm B (1/45, AR = 2.2%); both dormitories were located on the same floor. The first case developed symptoms on 14 October 2012, while the onset of the last case was on 18 February 2013. Two cases were diagnosed after initiation of the screening programme. Four cases presented with skin abscesses and one presented with a left arm pustule only. Two required hospital admission and three required surgical treatments such as incision and drainage. Their family members were all asymptomatic.

# Carriers

There were 254 students and 81 staff members at the school during the investigation period. Of these, 240 students (94.5%) (including the five cases) and 81 staff members (100%) were screened during Phase 1; two students refused screening and 12 were either absent or had quit the school. Two students refused decolonization therapies.

Overall, four of the five cases (80%) and eight other students (3.3%) were confirmed as carriers. Eight of these 12 carriers lived in Dorm A (8/41, AR = 19.5%), two in Dorm B (2/45, AR = 4.4%) and two in Dorm C (2/41, AR = 4.9%). Screening specimens from staff members were all negative.

During Phase 1, two cases and seven carriers screened positive. Two initial cases that screened negative in Phase 1 and two student carriers from Dorm A confirmed during Phase 1 re-screened positive in Phase 2, suggesting poor compliance to therapy and possibly ongoing disease transmission among Dorm A students. During Phase 3, when all Dorm A students and the five cases were re-screened, one new carrier was identified; two cases (one that tested positive and one negative in Phase 2) and one other carrier (re-screened positive in Phase 2) also were identified as carrying CA-MRSA. These four carriers were re-screened in Phase 4 with one again confirmed as a carrier.

In summary, the number of carriers for CA-MRSA decreased from nine to one (**Table 1**) over the screening phases; from 25 March 2013, no further CA-MRSA infection cases were identified (**Figure 1**).

# Laboratory investigations

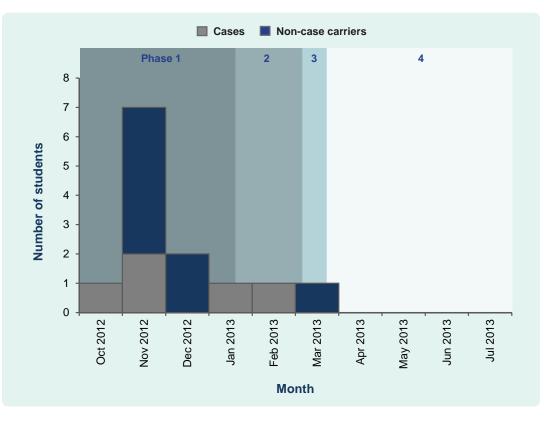
All case isolates (n = 5) and all screening isolates (n = 12) were of *spa* type t441 and were resistant to erythromycin and clindamycin but were sensitive to gentamicin, vancomycin and mupirocin.

# **Field investigations**

Seven field visits to the school occurred. Health talks during each field visit provided information to students and staff on disease, personal and environmental hygiene, advice on wound treatment and exclusion from sports. The school was advised to conduct terminal cleansing during the Easter holiday (28 to 29 March 2013) when all dormitories were vacated.

Substantial mixing opportunities in the dormitories, bathrooms, laundry and common areas (e.g. gymnasium)





CA-MRSA – Community-associated methicillin-resistant Staphylococcus aureus

# Box 1. Deficiencies identified and control measures advised in School X regarding the CA-MRSA outbreak, Hong Kong (China), November 2012 to July 2013

| Observations  | Recommendations  |
|---|--|
| Student Dormitories<br>Bunk beds separated by one metre of space without partition.<br>Social gatherings often held on the beds. Linen and blankets<br>not washed and changed regularly.  | Wash and change linen and blankets weekly and provide alcohol-based hand sanitizers in each dormitory.   |
| <b>Bathrooms and lavatories</b><br>Shared facilities among each dormitory. Wet towels of different<br>students hung closely or overlapped on hanging racks with<br>reports of sharing towels. Hand-washing soap not provided and<br>curtains at the entrances not washed regularly. Carpets placed<br>near entrances. Lockers in bathrooms not partitioned. | Space out and separate towel hooks using labelled partitions<br>to avoid cross-contamination and provide liquid soap and hand<br>dryer/disposable paper towel. Discard or wash very frequently<br>all curtains and carpets at entrances. Install partitions for<br>lockers to avoid cross-contamination of personal items. |
| <b>Common areas</b><br>Equipment in gymnasium (e.g. dumbbells and gym mattresses)<br>not disinfected after use. A sofa shared by all students had<br>no removable/washable cover and was difficult to clean.<br>Frequently touched surfaces such as stair-rails and lamp<br>switches not cleaned regularly.   | Minimize shared use of equipment in gymnasium and disinfect<br>between uses. Provide easy-to-clean and removable cover<br>for sofa to be changed regularly. Clean frequently touched<br>surfaces at least twice daily with diluted (1:49) bleach.  |
| <b>Cleansing and laundry equipment</b><br>Mops and cleansing towels not disinfected and dried after use.<br>Dirty and clean linen were placed together in buckets.  | Disinfect and dry mops and cleansing towels after use. Label separate buckets for dirty and clean laundry. Wash all laundry from Dorm A using hot water cycle (up to 90 °C for 45 minutes) during outbreak period.   |

were identified. Deficiencies in hand-hygiene facilities and awareness and suboptimal environmental and personal hygiene were possible factors for CA-MRSA transmission in School X (**Box 1**). Staff of School X were also asked to supervise non-compliant students for decolonization therapy to intensify outbreak control.

# DISCUSSION

We reported a CA-MRSA outbreak affecting five students in a boarding school in which two (40%) were hospitalized and three (60%) required surgical treatment; this was the largest institutional CA-MRSA outbreak recorded in Hong Kong (China). In the early phases of outbreak control, despite repeated field inspections, universal screening and decolonization therapies in the school, compliance to decolonization therapy and progress on environmental interventions remained suboptimal. Two cases initially screened negative in the first phase were detected as carriers in the second phase, indicating possible ongoing transmission.

A regimen of intranasal mupirocin and chlorhexidine body wash have been found to eradicate CA-MRSA colonization in more than 80% of carriers in Hong Kong (China).<sup>4</sup> This decolonization regime was adopted early in the control of this outbreak, but compliance appeared to be poor as one new case and subsequent carriers were identified. Supervised decolonization therapy was then adopted as part of intensified measures together with reinforcement of environmental and personal hygiene control. Intensive cleaning of the school during the school holidays in March 2013 and weekly surveillance to ensure early identification and prompt treatment of potential skin lesions, as per a previously reported outbreak,<sup>2</sup> were also adopted. The outbreak was contained after such coordinated efforts and interventions.

Previous local studies suggested that sharing of personal items is a risk factor, while good hand hygiene may protect against infection.<sup>5</sup> In this outbreak, most cases (4/5, 80%) and carriers (5/8, 62.5%) lived in the same dormitory with shared use of facilities. Field investigations also revealed suboptimal hygiene practices which may have facilitated transmission within, and to a lesser extent between, dormitories in the school.

CA-MRSA isolates in Hong Kong (China) have been predominantly of spa type t019 and t437,<sup>6</sup> different to the spa type t441 identified in this outbreak. However, the latter has occasionally been found in other Asian countries and is closely related to t437,<sup>7</sup> belonging to the same lineage (sequence type 59, the Taiwan [China] clone).<sup>8</sup>

For future outbreaks, we recommend that systematic data be collected in each phase (e.g. hand hygiene and decolonization compliance) for quantitative analysis of the effectiveness of individual control measures.

# **CONCLUSION**

We reported a CA-MRSA outbreak affecting five students in a boarding school in Hong Kong (China). Identification of carriers, decolonization therapy, intensive monitoring of cases and contacts and strengthening of environmental and personal hygiene were important strategies to help contain this school outbreak.

# *Conflict of interest*

None declared.

# Funding

None.

# Acknowledgements

We would like to thank all staff of the Surveillance and Epidemiology Branch of the Centre for Health Protection who contributed in the investigation and control of this outbreak. We would also like to thank Alain Moren and Marta Valenciano for their advice in report writing.

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# National dengue surveillance in the Lao People's Democratic Republic, 2006–2012: epidemiological and laboratory findings

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Although dengue has been a public health problem for several decades in the Lao People's Democratic Republic, the magnitude of the disease burden and epidemiological trends remain poorly understood. We analysed national dengue surveillance and laboratory data from 2006 to 2012 by person, place and time. Between 2006 and 2012, the annual dengue notification rate ranged between 62 and 367 cases per 100 000 population with an apparent geographical expansion of transmission throughout the country in recent years and concurrent co-circulation of all four dengue virus subtypes. An electronic database, called Lao Early Warning Alert and Response Network, was introduced in 2008 to provide automated early warning for outbreaks and epidemics. Village outbreaks continue to be notified primarily through event-based surveillance, whereas the weekly indicator-based system provides systematic assessment of annual epidemic cycles. The dengue case data indicate a high and increasing burden of disease. Efforts now need to focus on using available data to prompt more effective outbreak response and to guide the design and implementation of intervention strategies.

Dengue is the most rapidly spreading mosquitoborne viral disease in the world; the disease is caused by infection with one of four related viral serotypes (DEN1–4), vectored primarily by *Aedes aegypti* mosquitoes. It was recently estimated that there are 390 million dengue infections per year worldwide, with more than two thirds of the burden being borne by Asia.<sup>1</sup>

The Lao People's Democratic Republic is one of the least developed countries of South-East Asia, with an estimated population of only 6.5 million in 2012 living in predominantly rural agricultural communities. The country is landlocked, but there are increasing trade and traffic linkages with other dengue-endemic neighbouring countries. In 2013, the country experienced the worst dengue fever epidemic on record; consistent with global dengue emergence, the local patterns of transmission appear linked to increasing urbanization.<sup>2</sup> Although dengue has been a public health problem for several decades in the Lao People's Democratic Republic,

with high levels of endemicity, in urban and periurban areas, the magnitude of the disease burden and epidemiological trends remain poorly understood. In this report we summarize national dengue surveillance and laboratory data over a seven-year period (2006–2012).

# **METHODS**

Dengue surveillance in the Lao People's Democratic Republic is included within the indicator-based National Surveillance System for Notifiable Selected Diseases that consists of passive weekly reports of clinically suspected cases, on admission, from all health-care facilities across the country. The case data comprise gender, age, date of onset, geographic locators (village, district, province) and case severity classifications. Between 1998 and 2010, dengue case definitions were based on the 1997 WHO guidelines<sup>3</sup> for dengue fever, dengue haemorrhagic fever and dengue shock syndrome. From 2011, revised WHO case classifications<sup>4</sup> were adopted: dengue without warning signs, dengue with

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Submitted: 6 January 2014; Published: 31 March 2014 doi: 10.5365/wpsar.2014.5.1.001

warning signs or severe dengue (SD). Data reporting was paper-based until 2008, when an electronic database with automated early warning alerts was introduced called Lao Early Warning Alert and Response Network (Lao EWARN). Data inputted into Lao EWARN consist of weekly case numbers and deaths stratified by case classification and aggregated by province and district. Outbreak alerts are signalled when the number of dengue cases exceeds the historical mean or whenever one or more suspected cases of SD are reported. Epidemic alerts are signalled when case numbers exceed two standard deviations above the historical mean. Historical means are usually based on five years of reported data (epidemic years are excluded). Epidemic years are defined as those with reported dengue cases markedly over epidemic thresholds throughout the dengue season and/or when the health care system is overwhelmed (i.e. a shortage of hospital beds).

The National Center for Laboratory and Epidemiology (NCLE) has maintained a database of outbreaks since 2007 that includes outbreaks identified by health workers and community members (event-based surveillance) and outbreaks identified through the Lao EWARN system. When suspected dengue outbreaks are notified, response teams may be sent to collect sera from a target of 10 acute cases (fever onset less than seven days). Onsite field testing of sera using rapid diagnostic tests (RDTs) is performed if kits are available. Specimens are transferred to NCLE on wet ice by bus or air for further laboratory diagnostics. Between 2006 and 2012, laboratory diagnosis of dengue at NCLE was conducted by dengue IgM and IgG RDTs (various suppliers), commercial dengue IgM and IgG capture enzyme-linked immunosorbent assay (ELISA) (Panbio, Australia), haemagglutination inhibition assays (for epidemiological serosurveys only)<sup>5</sup> and real-time polymerase chain reaction (RT-PCR). RDT kits including NS1 antigen (Dengue Duo NS1 Antigen + IgM/IgG, Standard Diagnostics Inc., Republic of Korea) were introduced from late 2009 and dispatched to the field. Molecular serotyping by RT–PCR was first introduced in 2006, using a conventional two-step assay performed on acute sera,<sup>6</sup> and a real-time RT–PCR protocol was adopted in 2012.<sup>7</sup> Starting in 2007, a testing algorithm was adopted whereby all sera submitted for analysis were tested by IgM capture ELISA, and a subset representing geographically diverse outbreaks were screened by RT-PCR. Cases were considered laboratory confirmed if the sera were processed at NCLE and tested positive for dengue IgM

antibodies by ELISA or for dengue virus via RT–PCR. Convalescent sera were only rarely collected and tested.

Case data presented here comprise data extracted from the Lao EWARN database available from 2006 and validated in 2013. Case fatality rates (CFRs) were estimated based on the ratio of deaths to total reported cases. Age and gender of suspected cases were only actively collected from provinces by NCLE during the dengue epidemic in 2010. Laboratory data were extracted from log books going back to 2000. The results from the RDTs containing NS1 antigen were not available for analysis. Descriptive analyses were conducted using Excel, Epi Data Analysis v2.2 and ArcView. The chisquare test was used for bivariate analyses.

# RESULTS

# **Descriptive epidemiology**

Between 2006 and 2012, the annual dengue notification rate ranged between 62 and 367 cases per 100 000 population (Table 1). The CFR was 0.2% for all years except for 2008 when it was significantly higher at 0.5% (P < 0.01). In the epidemic year of 2010, 22 890 cases and 46 deaths were reported (estimated 367 cases per 100 000 population). The largest number of cases occurred among 10- to 20-year-olds (34%) with significantly more males (12 000 cases) than females (9119 cases, P < 0.01); male–female ratio: 1.3:1 (Figure 1). Case reporting by province for 2008 to 2012 indicated a marked expansion of geographic range (Figure 2). The number of provinces with a notification rate  $\geq$  200 per 100 000 increased from one in 2006–2008 to five in 2009 and to 10 in 2010 (the first year that all provinces in the country reported dengue cases). Two provinces had notification rates of  $\geq$  200 per 100 000 in 2011, and in 2012 this increased to six provinces. Outbreaks were reported almost exclusively from urban and peri-urban areas and only rarely from more remote rural villages.

Case reporting was highest from May/June to October/November with peaks in late August or September. In 2008, cases peaked earlier in June, and in 2012 cases peaked in October. Between the years 2006 and 2009, the outbreak alert threshold was exceeded every week during May through November, but the epidemic threshold was reached for only one to two weeks at a time. In contrast, in 2010, reported dengue

# Table 1. Notifiable disease surveillance case reporting of suspected dengue cases and notification rate per 100 000, Lao People's Democratic Republic, 2006–2012

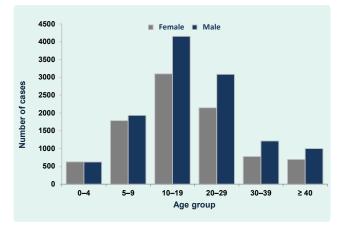
| Year  |         | Reported de | ngue cases |        | Deaths  | CFR  | Notification rate |
|-------|---------|-------------|------------|--------|---------|------|-------------------|
| . oui | DF/D-WS | DHF/D+WS    | DSS/SD     | Total  | Doutilo |      | per 100 000*      |
| 2006  | 5 046   | 664         | 71         | 5 781  | 11      | 0.19 | 101               |
| 2007  | 4 665   | 593         | 132        | 5 390  | 10      | 0.19 | 92                |
| 2008  | 4 248   | 181         | 58         | 4 487  | 21      | 0.47 | 75                |
| 2009  | 6 383   | 807         | 83         | 7 273  | 14      | 0.19 | 119               |
| 2010  | 20 986  | 1 639       | 265        | 22 890 | 46      | 0.20 | 367               |
| 2011  | 3 835   | 52          | 19         | 3 906  | 7       | 0.18 | 62                |
| 2012  | 9 386   | 514         | 52         | 9 952  | 22      | 0.22 | 154               |

CFR – case fatality rate; DF/D–WS – dengue fever/dengue without warning signs; DHF/D+WS – dengue haemorrhagic fever/dengue with warning signs; DSS/SD – dengue shock syndrome/severe dengue.

\* Based on population prediction of the Lao People's Democratic Republic National Census 2005.

cases exceeded the epidemic threshold consistently from week six to week 45 (39 weeks duration) (**Figure 3**). Case reporting was exceptionally low and the outbreak threshold was only crossed twice in 2011. In 2012,

# Figure 1. Suspected dengue cases stratified by age group and sex, Lao People's Democratic Republic, 2010



cases exceeded the epidemic threshold for 16 weeks from week 35 onwards.

Between 2007 and 2012, a total of 323 outbreaks were notified (all causes), and dengue was suspected in 41 (13%) events (**Table 2**). In total, 76% (31/41) of dengue outbreak investigations included specimen collection (at least one sample) and 81% (25/31) were laboratory confirmed at NCLE. In 2010, 11 of 35 (31%) outbreaks were suspected dengue, and 3 of 7 (43%) outbreaks were confirmed. In 2012, all suspected dengue outbreaks (n = 14) led to investigations and sample submissions, with 13 of 14 outbreaks confirmed. Most outbreaks were notified through ad hoc event-based surveillance rather than via Lao EWARN.

# Laboratory testing and serotype distribution

From 2000 to 2006, an average of 20 sera per year from suspected dengue cases were submitted for



| Year  | Total outbreaks<br>reported<br>(all causes) | outb | dengue<br>reaks<br>otal) | No. of<br>dengue cases<br>reported | No. of dengue<br>outbreaks with<br>specimens<br>submitted | No. of dengue<br>outbreaks with<br>>10 specimens<br>submitted | No. of dengue<br>outbreaks with at<br>least one sample<br>laboratory confirmed |
|-------|---|------|--------------------------|------------------------------------|---|---|--|
| 2007  | 15  | 0    | (0)                      | NR                                 | 0   | 0   | 0  |
| 2008  | 15  | 3    | (20)                     | NR                                 | 3   | 1   | 3  |
| 2009  | 66  | 9    | (14)                     | 140*                               | 4   | 3   | 3  |
| 2010  | 35  | 11   | (31)                     | 227                                | 7   | 3   | 3  |
| 2011  | 50  | 4    | (8)                      | 94                                 | 3   | 1   | 3  |
| 2012  | 142   | 14   | (10)                     | 1926                               | 14  | 4   | 13   |
| Total | 323   | 41   | (13)                     | 2387                               | 31  | 12  | 25   |

NR - not recorded

\* Cases recorded for four of nine reported outbreaks.



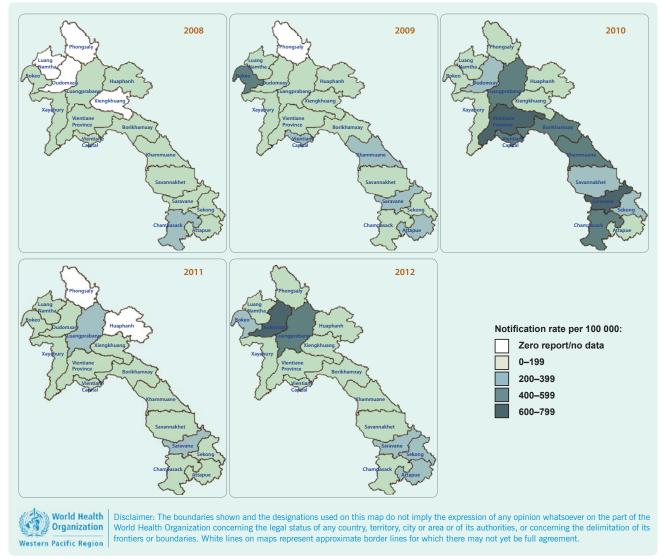
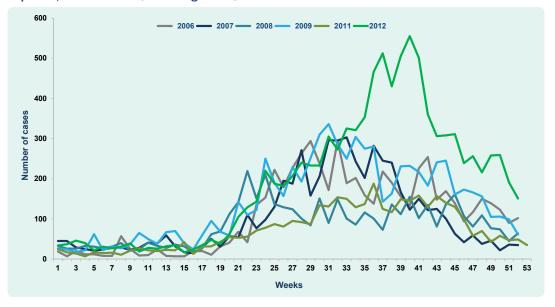


Figure 3. Total number of suspected dengue cases by week in non-epidemic years, Lao People's Democratic Republic, 2006–2012 (excluding 2010)



|      | No. of samples | No. to | sted* |         | Rapi  | d test  |       |          | ELI  | SA     |        | RT-PCR pc | oitiv |    |  |
|------|----------------|--------|-------|---------|-------|---------|-------|----------|------|--------|--------|-----------|-------|----|--|
| Year | received at    | NO. LE | sted  | IgM pos | itive | IgG pos | itive | IgM posi | tive | lgG po | sitive | кт-РСКро  | Siliv |    |  |
|      | NCLE           |        | %     | n       | %     | n       | %     | n        | %    | n      | %      | n         | %     |    |  |
| 2000 | 16             | 10     | 62    | 1/10    | 10    | 1/10    | 10    | ND       |      | N      | C      | ND        |       |    |  |
| 2001 | 89             | 45     | 50    | 12/45   | 28    | 16/45   | 35.6  | ND       |      | ND     |        | ND        |       | ND |  |
| 2002 | 54             | 25     | 46    | 7/25    | 28    | 13/25   | 52    | ND       |      | ND     |        | ND        |       |    |  |
| 2003 | 40             | 24     | 60    | 8/24    | 33    | 12/24   | 50    | ND       |      | ND     |        | ND        |       |    |  |
| 2004 | 23             | 7      | 30    | 1/7     | 14    | 1/7     | 14.3  | ND       |      | ND     |        | ND        |       |    |  |
| 2005 | 5              | 4      | 80    | 2/4     | 50    | 1/4     | 25    | ND       |      | ND     |        | ND ND     |       |    |  |
| 2006 | 31             | 25     | 80    | No da   | ta    | No da   | ata   | 20/25    | 80   | 14/25  | 56.0   | ND        |       |    |  |
| 2007 | 178            | 124    | 69    | 13/28   | 45    | 11/28   | 39    | 93/124   | 75   | 52/77  | 67.5   | 66/179    | 37    |    |  |
| 2008 | 365            | 365    | 100   | 32/81   | 39    | 29/81   | 35    | 145/307  | 47   | N      | C      | 63/172    | 37    |    |  |
| 2009 | 530            | 506    | 95    | 126/257 | 49    | 96/257  | 37    | 115/258  | 44   | N      | C      | 25/48     | 52    |    |  |
| 2010 | 733            | 733    | 100   | 52/127  | 41    | 50/127  | 39    | 449/729  | 61   | N      | C      | 90/131    | 69    |    |  |
| 2011 | 111            | 111    | 100   | 0/2     | 0     | 0/2     | 0     | 49/111   | 44   | N      | C      | 8/26      | 31    |    |  |
| 2012 | 852            | 852    | 100   | ND      |       | ND      |       | 432/852  | 51   | N      | C      | 109/242   | 45    |    |  |

#### Table 3. Laboratory diagnosis of suspected dengue cases referred NCLE, 2000–2012

\* Reflects the number of sera processed by any diagnostic test (rapid test, ELISA and/or RT-PCR).

ELISA – enzyme-linked immunnosorbent assay; NCLE – National Center for Laboratory and Epidemiology; ND – not done; RT-PCR – real-time polymerase chain reaction.

|            | Suspected cases | Laboratory-confirme<br>cases (%) |      |  |  |  |
|------------|-----------------|----------------------------------|------|--|--|--|
| Total      | 2591            | 1190                             | 45.9 |  |  |  |
| Age groups |                 |                                  |      |  |  |  |
| 0–4        | 133             | 66                               | 49.6 |  |  |  |
| 5–9        | 434             | 224                              | 51.6 |  |  |  |
| 10–19      | 911             | 439                              | 48.2 |  |  |  |
| 20–29      | 555             | 241                              | 43.4 |  |  |  |
| 30–39      | 270             | 122                              | 45.2 |  |  |  |
| ≥ 40       | 251             | 85                               | 33.9 |  |  |  |
| Unknown    | 33              | 13                               | 39.4 |  |  |  |
| Sex        |                 |                                  |      |  |  |  |
| Male       | 1278            | 604                              | 47.3 |  |  |  |
| Female     | 1294            | 579                              | 44.7 |  |  |  |
| Unknown    | 19              | 7                                | 36.8 |  |  |  |

# Table 4. Total number of laboratory-confirmed dengue cases by age and sex, 2008–2012

analysis (**Table 3**). These specimens comprised referrals from provincial hospitals and samples from outbreak investigations. Specimen referrals increased steadily from 2007 and 2010, reaching a total of 733 specimens in 2010, dropping in 2011 due to low case numbers and increasing again in 2012 to 852 specimens. The number of laboratory-confirmed dengue samples by age and sex aggregated from 2008 to 2012 are presented in **Table 4**. There was a lower proportion of laboratory-confirmed dengue in the 40-years-and-older age group

(33.9%, P < 0.01) compared to younger age groups (43.4–51.6%). Since the establishment of in-house molecular serotyping in 2006, a total of 798 sera have been processed by RT–PCR. All four serotypes were detected in 2008, 2009 and 2010 (**Table 5**). Serotype 1 was the predominant serotype detected in the period 2007–2011, and serotype 3 (n = 102/109, 94%) was the most frequent in 2012.

# DISCUSSION

The dengue case data from the Lao People's Democratic Republic indicate a high and increasing burden of disease as evidenced by the annual notification rate (62–367 cases per 100 000 population), numbers of outbreak alerts, the concurrent co-circulation of all four dengue virus subtypes and the explosive nationwide epidemic in 2010 (**Table 1**). A trend of increasing emergence is similar to that reported from neighbouring countries; in 2010, the Lao People's Democratic Republic had the highest notification rate in the Western Pacific Region.<sup>8</sup>

Fluctuations in severity of disease over the surveillance period, such as the significantly higher CFR in 2008, are difficult to explain. Given the changes to dengue case definitions in 2011, interpretation of trends over the surveillance period should be made with caution. Development of statistical approaches to correct for the impact of these modifications would be a

| Year | Total no. |     | RT-PCR | positive | DE | N1 | DE | N2  | DE | N3 | DE | N4 |
|------|-----------|-----|--------|----------|----|----|----|-----|----|----|----|----|
| Tear | tested    | n   | %      | n        | %  | n  | %  | n   | %  | n  | %  |    |
| 2007 | 179       | 66  | 37     | 48       | 73 | 0  |    | 8   | 12 | 10 | 15 |    |
| 2008 | 172       | 63  | 37     | 23       | 37 | 17 | 27 | 5   | 8  | 18 | 29 |    |
| 2009 | 48        | 25  | 52     | 13       | 52 | 2  | 8  | 3   | 12 | 7  | 28 |    |
| 2010 | 131       | 90  | 69     | 34       | 38 | 27 | 30 | 20  | 22 | 9  | 10 |    |
| 2011 | 26        | 8   | 31     | 6        | 75 | 1  | 13 | 1   | 13 | 0  | _  |    |
| 2012 | 242       | 109 | 45     | 1        | 1  | 6  | 5  | 102 | 94 | 0  | _  |    |

Table 5. Molecular serotyping of dengue cases, Lao People's Democratic Republic, 2007–2012

RT-PCR – real-time polymerase chain reaction.

useful contribution for countries with such discrepancies in national data sets. Although our finding of an excess of male suspected dengue cases in 2010 is consistent with a recent assessment of gender distribution in one province in the Lao People's Democratic Republic,<sup>9</sup> we found no significant difference in laboratory-confirmed cases.

Provinces with large cities and high levels of rural-urban migration regularly reported the highest case numbers. More rural and isolated provinces, however, also had higher notification rates from 2009. One outbreak in a remote village in Xayabury Province during the dry season was particularly noteworthy because the serotype was genotypically endemic DEN1, but ecological factors suggested the possibility of sylvatic transmission.<sup>10</sup> Expansion of dengue to rural areas should be closely monitored as these populations are particularly vulnerable with poor access to healthcare facilities. As seen in most dengue-endemic countries, disease transmission is highly seasonal in the Lao People's Democratic Republic and coincides with the wet season. To date, the national case data do not suggest a clear pattern of epidemic cycles as has been found elsewhere in the Region.<sup>11,12</sup>

The data presented here suggest a trend of increased transmission and geographic expansion (Figure 2) throughout the country as has been seen across the region.<sup>8</sup> However, the apparent dengue disease emergence may be partly explained by ascertainment bias introduced by ongoing evolution of the surveillance infrastructure. Dengue case reporting in the Lao People's Democratic Republic has surely been influenced by national awareness and community education campaigns, changing health-seeking behaviour and improved access to telecommunications. Increased awareness of dengue was evidenced by trends in outbreak notifications (Table 2) and increases in specimen referral

(Table 3). Development of the Lao EWARN system in 2008 facilitated automated tracking in real time and for the first time enabled data validation exercises and timely feedback to health offices to encourage regular reporting. However, the current surveillance system still has numerous inherent limitations including poor access to health-care facilities, clinical and laboratory misdiagnosis through confounding dengue with other diseases<sup>13,14</sup> and underreporting of deaths due to cultural preferences for family members to die at home. Moreover, internal evaluations of the surveillance system have found inconsistent use of clinical case definitions and weekly variability in the number of sites reporting each week; there is not yet a system to link laboratory test results to case reporting nor a systematic reporting of RDT results during outbreak investigations. Molecular serotyping results for the period were likely biased towards outbreak samples as these were more frequently sampled and sequenced than routine referral samples.

The dengue surveillance system in the Lao People's Democratic Republic has made extraordinary progress and currently meets many of the key international recommendations for surveillance and outbreak response. The outbreak alerts that are triggered regularly via Lao EWARN during epidemic years tend to overwhelm provincial and district health offices, and resources are often insufficient to verify and investigate all alerts. Hence, village outbreaks continue to be notified primarily through event-based surveillance, whereas the weekly indicator-based system provides systematic assessment of annual epidemic cycles. The NCLE, the Lao Oxford Mahosot Hospital Wellcome Trust Research Unit and Institute Pasteur have initiated systematic virological testing of dengue samples from several sentinel provinces; RDT results are now being reported from the field, the serotype/sequence database on dengue is accumulating, and a new working group has been established to coordinate analysis and interpretation

of dengue data. The forthcoming analyses will assist in the critical task of designing and implementing effective preparedness and interventions strategies, including contingency plans and risk assessment schemes, and guiding policy-makers in making decisions on vaccine introduction when available.

# Conflicts of interest

None declared.

# Funding

None.

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# Sustained outbreak of measles in New South Wales, 2012: risks for measles elimination in Australia

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Objective: On 7 April 2012, a recently returned traveller from Thailand to Australia was confirmed to have measles. An outbreak of measles subsequently occurred in the state of New South Wales, prompting a sustained and coordinated response by public health authorities. The last confirmed case presented on 29 November 2012. This report describes the outbreak and its characteristics.

Methods: Cases were investigated following Australian protocols, including case interviews and assessment of contacts for post-exposure prophylaxis.

Results: Of the 168 cases identified, most occurred in south-western and western Sydney (92.9%, n = 156). Notable features of this outbreak were the disproportionately high number of cases in the 10–19-year-old age group (29.2%, n = 49), the overrepresentation among people of Pacific Islander descent (21.4%, n = 36) and acquisition in health-care facilities (21.4%, n = 36). There were no reported cases of encephalitis and no deaths.

Discussion: This was the largest outbreak of measles in Australia since 1997. Its occurrence highlights the need to maintain vigilant surveillance systems for early detection and containment of measles cases and to maintain high population immunity to measles through routine childhood immunization. Vaccination campaigns targeting susceptible groups may also be necessary to sustain Australia's measles elimination status.

easles is a highly infectious disease caused by a paramyxovirus of the genus Morbillivirus. Globally it is the most important cause of vaccine-preventable death.1 In Australia, two doses of measles-mumps-rubella (MMR) vaccine were introduced to the routine childhood vaccination schedule in 1998 for all children at 12 months and four years of age and for all adults born after 1966 who were not immune or had one dose of MMR.<sup>2</sup> Since July 2013, the second dose has been administered at 18 months of age as the measles-mumps-rubella-varicella (MMRV) vaccine.<sup>3</sup> A measles control campaign was also adopted in 1998, targeting children aged five to 12 years, resulting in high two-dose vaccination rates for this group. A national serological survey in 2002 estimated that the cohort born between 1978 and 1982 (aged 30-34 years in 2012) had lower immunity, having only received one dose of measles vaccine and being born in a period when natural measles infection was less common; the cohort born before 1978 had better immunity.<sup>4</sup> Those born before 1966 were assumed to have been naturally infected.

Measles elimination has been discussed since the development of an effective measles vaccine in the 1960s. In 2005, the World Health Organization Regional Committee for the Western Pacific, of which Australia is a member, formally declared a goal of measles elimination in the region by 2012.<sup>5</sup> It has been suggested that this had been achieved in Australia as early as 1999,<sup>4</sup> due to high population immunity achieved through the 1998 measles control campaign and ongoing high two-dose vaccination rates among children since then,<sup>4,6</sup> as well as a low incidence rate of measles in Australia with no endemic genotypes of the virus found in Australia since the early 1990s.<sup>4,7</sup>

However, measles cases acquired overseas are still detected in Australia which occasionally results in small outbreaks with ongoing transmission occurring in under-immunized populations. A large measles outbreak began in April 2012, with the index case being a 25-year-old male traveller from Thailand. During the next eight months, a further 167 cases were identified in the Australian state of New South Wales (NSW),

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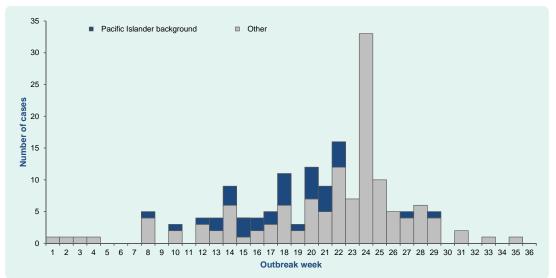
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Submitted: 14 October 2013; Published: 30 January 2014

doi: 10.5365/wpsar.2013.4.4.002

# Figure 1. Number of measles cases by outbreak week and Pacific Islander status by symptom onset date, New South Wales, Australia, April to November 2012 (n = 168)



constituting the largest measles outbreak in Australia since 1997 and illustrating the challenges in maintaining Australia's measles elimination status. We report on the characteristics of this outbreak.

# **METHODS**

Under the NSW Public Health Act 2010,<sup>8</sup> patients with measles must be notified to the local Public Health Unit by doctors and laboratories. NSW is divided into eight Local Health Districts with each district containing a Public Health Unit. Local Health Districts are subdivided into Local Government Areas (LGAs) and further subdivided into suburbs.

All confirmed cases, as defined in the Australian national guidelines,<sup>9</sup> with a symptom onset between 7 April and 29 November 2012, an epidemiological link to South Western Sydney or Western Sydney Local Health Districts, no history of overseas travel and a laboratory specimen that was of either unknown or D8 genotype were considered part of the outbreak. Clinical specimens from measles cases occurring in this period with no clear epidemiological link to outbreak cases underwent genotyping at a reference laboratory.

Routine case investigation and the public health response followed the Australian national guidelines.<sup>9</sup> Where possible, vaccination status was validated on the Australian Childhood Immunization Register (ACIR) established in 1996 to record immunizations administered to children under the age of seven. ACIR is considered to be a reliable record of all immunizations received in Australia by Australian residents currently aged 16 and under. Contacts of cases were assessed for timely post-exposure prophylaxis, either MMR or human normal immunoglobulin, as indicated.

Data were analysed using Microsoft Excel 2010 and Epi Info<sup>™</sup> 7. Age-specific notification rates were calculated using 2012 mid-year NSW population data from the Australian Bureau of Statistics. Crude notification rates for Aboriginal and/or Torres Strait Islander people and people of Samoan ancestry were calculated using NSW population data obtained in the 2011 national census. Data on MMR vaccination coverage by postcode and LGA were obtained from the NSW Ministry of Health. Mapping of cases was performed using ArcGIS 10.1.

# RESULTS

# Temporal and geographic distribution

Between April and November 2012, over a period of 36 weeks, 168 confirmed cases of measles occurred in NSW (**Figure 1**) – the majority (n = 126, 75.0%) in South Western Sydney Local Health District (**Figure 2**). Western Sydney Local Health District had the next highest number of cases (n = 30, 17.9%), with the remaining cases distributed among several other districts. LGAs with the highest notification rates were Campbelltown, Camden and Liverpool (**Table 1**), all located in South Western Sydney Local Health District.

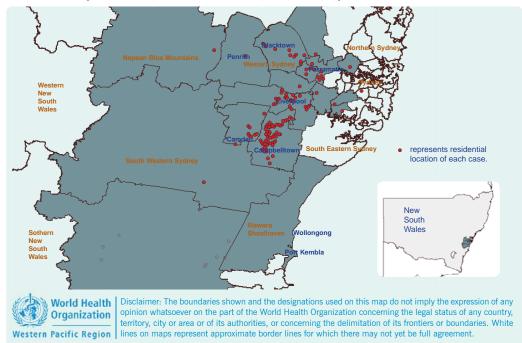


Figure 2. Measles cases by residence, New South Wales, Australia, April to November 2012 (n = 168)

Table 1. Measles case notification rates and immunization coverage rates with MMR1 and MMR2 in 2012in Local Government Areas in New South Wales with greater than 10 outbreak cases, April to<br/>November 2012

| Local Government Area                 | Incidence rate<br>(per 100 000 population) | MMR1 vaccination coverage at two years of age in 2012 (%) | MMR2 vaccination coverage at five years of age in 2012 (%) |
|---------------------------------------|--|---|--|
| Blacktown LGA                         | 3.2  | 93.7  | 91.0   |
| Camden LGA                            | 17.4                                       | 96.8  | 94.1   |
| Campbelltown LGA<br>Claymore (suburb) | 47.2<br>393.0                              | 94.8<br>92.6  | 92.3<br>88.2   |
| Liverpool LGA                         | 16.4                                       | 93.9  | 92.1   |
| Parramatta LGA                        | 5.7  | 93.2  | 91.0   |
| NSW (total)                           | 2.3  | 93.8  | 91.2   |

MMR – measles-mumps-rubella

The suburb of Claymore, located within Campbelltown LGA, had a particularly high notification rate (**Table 1**).

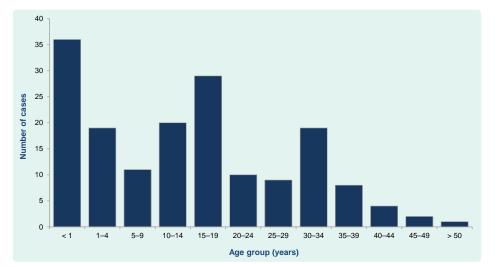
### **Case characteristics**

Approximately half the cases were male (n = 87, 51.8%), with the age ranging from four months to 61 years and a median age of 14 years (**Figure 3**). Measles case notification rates were highest in the less-than-one-year age group (n = 36, 37.3 per 100 000 population) followed by 15–19-year-olds (n = 29, 6.2 per 100 000 population), one- to four-year-olds (n = 19, 5.0 per 100 000 population) and 10–14-year-

olds (n = 20, 4.5 per 100 000 population). Among children aged less than one year (n = 36), 28% were aged less than nine months (n = 10).

Of the 168 cases, 12 (7.1%; 5.8 per 100 000 population) were identified as being Aboriginal and/or Torres Strait Islander people. Thirty-six cases (21.4%) were of Pacific Islander descent with 29 Samoan (17.3%; 188.7 per 100 000 population). The Pacific Islander cases were particularly overrepresented in the first half of the outbreak, with all but two occurring before week 23 (**Figure 1**). They also comprised 29% (n = 14) of the 10–19-year-old age group.

## Figure 3. Number of measles cases by age group, New South Wales, April to November 2012 (*n* = 168)



## Clinical course of illness

The most common symptoms recorded were rash (n = 168, 100%), fever (n = 165, 98.2%), cough (n = 158, 94.0%), coryza (n = 143, 85.1%) and conjunctivitis (n = 101, 60.1%). Koplik's spots were identified in 43 cases (25.6%), with other symptoms including lethargy, malaise, vomiting, sore throat and headache. Most cases (n = 130, 77.4%) had fever at the time of rash onset.

Forty-nine cases (29.2%) were hospitalized; seven (4.2%) developed complications – five developed bronchiolitis, one pneumonia and one pregnant case miscarried at eight weeks during the prodrome of her measles illness. There were no reported cases of encephalitis and no deaths.

### Laboratory diagnosis

Most cases (n = 157, 93.5%) were laboratory-confirmed with the remaining 11 cases (6.5%) confirmed based on clinical and epidemiological evidence. Of the 148 cases with available laboratory test results, most were confirmed through serological assay for measles virus-specific IgM antibodies (n = 123), followed by antigen detection on a respiratory specimen by immunofluorescence (n = 51) and nucleic acid testing on a respiratory or urine sample (n = 43). Negative test results were not reported to Public Health Units. Genotyping identified measles virus genotype D8 in 55 outbreak cases and genotype B3 in one case that was excluded from the outbreak.

### Vaccination

Forty cases (23.8%) reported a vaccination history of at least one dose of MMR. Of the 22 that were eligible for inclusion on ACIR, only seven were located on ACIR; three of the seven cases had received two doses of MMR vaccine. For the remaining 33 cases with no records on ACIR, only one provided alternate documentation of immunization status; the remaining 32 were based on self-report (six reported receiving two doses of MMR vaccine).

Most of the 128 cases that were not sure or reported no history of vaccination were aged more than one year (n = 95) and therefore were not vaccinated appropriately for their age. For the 52 cases that provided a reason for this non-vaccination, the most common reasons included being a vaccine refuser (n = 32), forgetting to get vaccinated (n = 5) or being born overseas (n = 3).

In 2012, the five LGAs with more than 10 outbreak cases (**Table 1**) had immunization coverage of at least 93% for the first dose of MMR vaccine and at least 91% for the second dose. The same was found by suburb, with the exception of Claymore in Campbelltown LGA which had coverage of 88.2% for the second dose of MMR.

## Health service presentations

There were 355 separate health service presentations by the 168 cases; 197 (55.5%) presented to

general practitioners and 158 (44.5%) to emergency departments. In 80 emergency department (50.6%) and 33 general practitioner (16.8%) visits, isolation procedures were adopted, and no contact follow-up was required. There were 16 instances of transmission occurring in the waiting rooms of general practices and emergency departments, and in hospital wards, resulting in 36 secondary cases (21.4% of all cases).

### Public health response

#### *Case and contact follow-up*

A total of 4786 contacts of cases not correctly isolated in waiting rooms of emergency departments and general practitioners were contacted by telephone and letter. Of these, 621 were advised to have MMR vaccine and 442 to have normal human immunoglobulin as post-exposure prophylaxis. An additional 415 personal contacts of cases were identified for follow-up; 80 were advised to have MMR vaccine and 85 to have normal human immunoglobulin.

The volume of cases and large number of susceptible contacts identified required additional staffing within some Public Health Units, and in South Western Sydney Local Health District Public Health Unit an Incident Command System structure was adopted. In addition, the NSW Health Computer Assisted Telephone Interviewing service was engaged to assist with contact follow-up.

#### Prevention measures

Multiple methods of communicating with both health practitioners and the community were used. Alerts were sent to general practitioners and emergency departments, local Public Health Units placed posters in areas believed to see a high volume of people within the most affected communities and multiple media releases were broadcast.

MMR vaccination clinics were established in seven high schools that either had confirmed cases or high enrolments of students of Pacific Islander descent. A community vaccination clinic was also established in a local club. In addition, Samoan churches were visited by public health staff and community leaders, and educational materials about measles were distributed in both English and Samoan.

# DISCUSSION

Despite high vaccination coverage and timely public health control measures, this measles outbreak continued for 35 weeks. In Australia, unvaccinated young adults have been linked to outbreaks and pose a particular risk because of their mobility, high contact rates and the increasing ease of overseas travel.<sup>10</sup> The D8 genotype in this outbreak is known to be circulating in Thailand and has been exported to Australia and Europe previously.<sup>11,12</sup> Key features of this outbreak were the disproportionately high notification rates in people of Pacific Island descent and teenagers. Other notable features included the number of infants affected and nosocomial transmission in health-care settings.

In the era of measles elimination, under-immunized minority groups are a major component of measles epidemiology; however, interventions to increase immunity in these groups remain a challenge.13-15 In Australia, Pacific Islanders are a high-risk group for ongoing transmission of measles,<sup>16</sup> as shown in this outbreak, where people of Pacific Island, particularly Samoan descent, were overrepresented. In 2006, there were approximately 100 000 Pacific Islanders living in Australia, predominantly in Sydney, Melbourne and Brisbane.<sup>17</sup> This figure, however, is likely to be an underestimate as many Pacific Islanders arrive via New Zealand, with which Australia has special mutual migration arrangements whereby citizens can visit, live and work in either country.<sup>18</sup> In the 2011 national census, Campbelltown LGA had a population of 145 967 with 2.1% reporting speaking Samoan in their households;<sup>19</sup> in Claymore, within Campbelltown LGA, this was 13.0% of the 3308 population, one of the highest proportions in NSW.<sup>20</sup> Official immunization data by ethnicity are not available, but staff that conducted the MMR clinics in high schools during the outbreak reported that many students of Pacific Islander background appeared to have missed routine childhood vaccinations both before and after their arrival in Australia.

The three LGAs with the highest notification rates in 2012, Campbelltown, Camden and Liverpool, also had higher vaccination coverage rates than the NSW average. This suggests that high coverage rates at the LGA level may not represent complete coverage within the LGA, as there may be pockets of under-immunized populations in these areas, as evidenced by the lower vaccine coverage

in Claymore. Therefore, as well as ensuring childhood vaccination targets of 95% for the first dose and 90% for the second dose,<sup>21</sup> geographically targeted strategies towards susceptible minority groups are also required to increase overall measles immunity.

There was also a high number of cases aged between 10 and 19 years in this outbreak – a group that should have received routine childhood vaccinations. A measles outbreak in England in 2012 showed a similar pattern, attributed to the dramatic fall in MMR vaccinations in the United Kingdom in the late 1990s following a link made between the MMR vaccine and autism, which was subsequently discredited.<sup>22</sup> However, this does not explain the high number of cases in this age group in this outbreak, as according to ACIR data, Australia did not suffer the same decline in MMR coverage at that time.<sup>23</sup> As ACIR data were not consistently reported until the late 1990s,<sup>24</sup> historical immunization coverage of teenagers (aged 14 and over in 2012) is not available. Also, the immunization status of children who migrate to Australia is not captured by ACIR, especially those over the age of four who have missed all routinely scheduled immunizations. These factors may partially explain why this potentially susceptible group that should have received routine childhood vaccinations may have been undetected before the outbreak. Despite this, that over two thirds of cases in this age group were born in Australia and should have received two doses of MMR vaccine as part of routine childhood immunizations introduced in 1998 is a concern.

Two other age groups at high risk of measles infection<sup>25</sup> were also overrepresented in this outbreak – infants and adults aged 30–34. Infants aged less than 12 months are too young to have been vaccinated. That a significant proportion of this group were aged less than nine months suggests earlier waning natural protection offered by maternal antibodies than previously thought.<sup>26</sup> Adults aged 30–34 years grew up in a period when measles was not endemic in Australia, but due to their age, they may have missed out on the 1998 vaccination programme and measles control campaign.

Nosocomial transmission in health-care settings formed a significant component of the outbreak burden, also seen in previous outbreaks,<sup>27</sup> as these settings are ideal for transmission of measles due to their closed spaces and susceptible occupants.<sup>28</sup> The large number of multiple presentations by cases to health-care facilities contributed to nosocomial transmission, as did the lack of isolation of cases presenting with a fever and rash, despite significant communication between public health authorities and clinical services. A high turnover of staff and the nature of shift work in emergency departments where staff were not always present to access the communications from public health authorities, as well as a lack of diagnostic experience among younger clinicians who often had never seen a case of measles, may explain these oversights.

There are some limitations to this outbreak investigation. Small surveillance gaps between generations of cases illustrated that not all cases of measles were being identified. Reporting of negative test results are not required in the established surveillance system, and cases that were initially notified but later discarded due to incomplete or poor-quality laboratory test results made it difficult to draw conclusions about the effectiveness of the surveillance system. Data quality was at times incomplete, including for ethnicity status and whether a contact received their recommended intervention. Cases were not followed up after initial interview and contact tracing; information about complications from measles was also incomplete and may underestimate the true burden of disease. The sensitive case definition used may have included cases not truly part of the outbreak; however, this number is likely to be small as all cases with no clear epidemiological links underwent genotyping with only one non-D8 case identified.

This outbreak, although the largest in Australia since 1997, was relatively modest in size, limited in geographical spread and of moderate duration compared with other recent outbreaks from industrialized countries throughout Europe.<sup>29</sup> However, its duration is cause for concern, particularly as recent modelling suggests that based on declining measles seropositivity, the effective reproductive number (R) may exceed one in Australia in the next few years.<sup>30</sup> Australia's measles elimination status was not affected by this outbreak; however, the circulation of a single measles virus genotype for 35 weeks highlights the need to maintain vigilant surveillance systems for early detection and containment of measles cases and to maintain high population immunity to measles. This outbreak also highlighted susceptibility of measles in Pacific Islanders living in Australia and that young travellers can cause measles outbreaks in non-endemic countries; a vaccination programmme targeting these at-risk groups needs to be implemented in conjunction with the routine childhood immunization programme, to which no change is required.

### Conflicts of interest

None declared.

### Funding

None.

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# Natural *Anaplasma phagocytophilum* infection in ticks from a forest area of Selenge province, Mongolia

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Anaplasma phagocytophilum is a zoonotic agent of public health importance, infecting both humans and animals. An investigation of the presence of Anaplasma phagocytophilum as well as Anaplasma platys was conducted in a forest area of Selenge province, Mongolia, where ticks are widely distributed and tick-borne diseases are highly endemic. Ticks were collected and tested using polymerase chain reaction based on *groEL* methodology. Anaplasma phagocytophilum was detected in 14 (6%) of *lxodes persulcatus* ticks and four (1%) *Dermacentor nuttalli* ticks; infection of Anaplasma platys was detected in 1% of *lxodes persulcatus* ticks and 10% of *Dermacentor nuttalli* ticks. The phylogenetic tree showed that the Anaplasma phagocytophilum clustered with the Russian group, most likely due to similar geographical locations. This finding is significant for both veterinary and public health officials given that these agents can cause both animal and human illness.

phagocytophilum naplasma is а gramnegative obligate intracellular bacterium long recognized as a veterinary agent<sup>1</sup> and more recently as a human infection. Human granulocytic anaplasmosis (HGA) was first reported in the United States of America in 1994,<sup>2</sup> and since then Anaplasma phagocytophilum has been considered an emerging pathogen of public health importance.<sup>3</sup> HGA is characterized by headache; chill; myalgia; arthralgia; malaise; and hematological abnormalities such as thrombocytopenia, leukopenia and elevated aminotransferase levels.<sup>4</sup> Anaplasma hepatic phagocytophilum is thought to be naturally maintained in a tick-rodent cycle with humans being involved only as incidental dead-end hosts.5

In Mongolia, livestock play an important role as reservoirs of *Anaplasma phagocytophilum* in endemic areas. The first study on human seroprevalence against *Anaplasma phagocytophilum* for central Asia reported a seroprevalence of 2.3% in Selenge province, 5.6% in Bulgan province, 2.8% in Dornogov province and 3.0% in both Tov province and Ulaanbaatar.<sup>6</sup>

The objective of this study was to investigate the presence of *Anaplasma phagocytophilum*in tick vectors in a forest area of Selenge province, Mongolia.

# METHODS

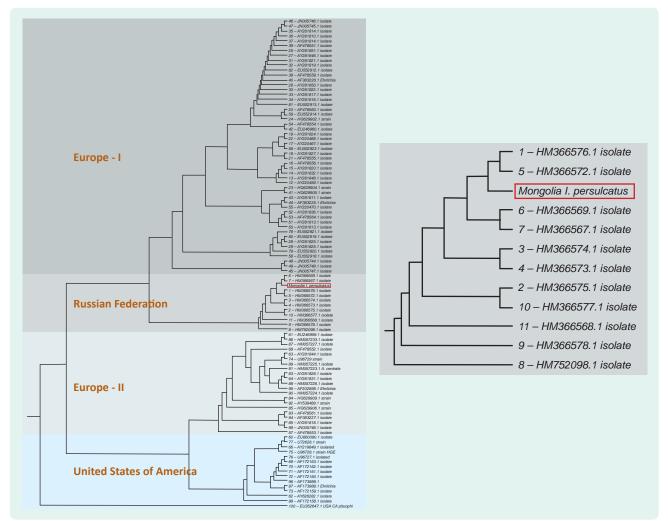
Un-engorged ticks were collected from two districts in Selenge province, Mongolia, Altanbulag and Khuder, both which border the Russian Federation. These districts were chosen for the study as they contain forest areas where ticks are widespread. Ticks were identified to the species level and stored alive at 4 °C until used. Tick samples (3–5 ticks) were frozen and mashed by liquid nitrogen and then deoxyribonucleic acid (DNA) was extracted using the G-spin genomic DNA extraction kit (iNrRON Biotechnology Inc., Republic of Korea).

Polymerase chain reaction (PCR) was conducted PCR-restriction using groEL fragment length polymorphism and sequence analysis.7 Primers designed to amplify the partial groEL gene encoding heat-shock protein of Anaplasma phagocytophilum EphplgroELF (5'-ATGGTATGCAGTTTGATCGC-3') and EphplgroELR (5'-TCTACTCTGTCTTTGCGTTC-3') were used and expected to yield a 625-bp product for Anaplasma phagocytophilum and for Anaplasma platys, respectively. PCR amplifications were performed using the Maxime PCR PreMix kit (iNrRON Biotechnology Inc., Republic of Korea). All PCR products were separated by agarose gel electrophoresis, stained with

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Submitted: 26 July 2013; Published: 5 March 2014 doi: 10.5365/wpsar.2013.4.3.001



#### Figure 1. Phylogenetic tree of Anaplasma phagocytophilum groEL gene

ethidium bromide and visualized under ultraviolet light (Figure 1).

Direct DNA sequencing was performed using the same PCR primers. If the sequence result was of low quality, the amplicon was cloned into a plasmid vector using a TOPO TA cloning kit (Invitrogen, Carlsbad, California) and then sequenced using the primers provided with the kit. Nucleotide sequences were initially checked using the Basic Local Alignment Search Tool hosted by the National Center for Biotechnology Information (http://blast.ncbi.nlm.nih.gov/Blast.cgim) for comparison with other known nucleotide sequences. The multiple alignment analysis and phylogenetic analysis were performed using the ClustalW online server (http://www.genome.jp/tools/clustalw/) with the default parameters.

# **RESULTS**

A total of 242 unfed ticks, comprising 222 adult *lxodes persulcatus* ticks and 20 adult *Dermacentor nuttalli* ticks, were collected and individually examined. Of these, 14 (6.3%) *lxodes persulcatus* samples and four (20%) *Dermacentor nuttalli* samples were positive for *Anaplasma phagocytophilum*; four (1.8%) *lxodes persulcatus* samples and two (10%) *Dermacentor nuttalli* samples were positive for *Anaplasma phagocytophilum*; for *Anaplasma platys* (Table 1).

The phylogenetic tree showed four main clusters: Europe-I, Russian Federation, Europe-II and United States of America (USA). The *Anaplasma phagocytophilum groEL* gene sequences from this study clustered within the Russian group and were most

| Tick species         | District   | Tick<br>gender | No. of samples | Positive for Anaplasma phagocytophilum (%) | Positive for Anaplasma<br>platys (%) |
|----------------------|------------|----------------|----------------|--|--------------------------------------|
| Dermacentor nuttalli | Altanbulag | Female         | 6              | 1 (16.7)                                   | -                                    |
| ( <i>n</i> = 20)     |            | Male           | 4              | 1 (25.0)                                   | -                                    |
|                      | Khuder     | Female         | 6              | 1 (16.7)                                   | 2 (33.3)                             |
|                      |            | Male           | 4              | 1 (25.0)                                   | -                                    |
|                      | Subtotal   | Female         | 12             | 2 (16.7)                                   | 2 (16.7)                             |
|                      |            | Male           | 8              | 2 (25.0)                                   | -                                    |
|                      |            | All            | 20             | 4 (20.0)                                   | 2 (10.0)                             |
| Ixodes persulcatus   | Altanbulag | Female         | 23             | 3 (13.0)                                   | 1 (4.4)                              |
| ( <i>n</i> = 222)    |            | Male           | 26             | 2 (7.7)                                    | 1 (3.8)                              |
|                      | Khuder     | Female         | 88             | 5 (5.7)                                    | 2 (2.3)                              |
|                      |            | Male           | 77             | 4 (5.2)                                    | -                                    |
|                      | Unknown    |                | 8              | -  | -                                    |
|                      | Subtotal   | Female         | 111            | 8 (7.2)                                    | 3 (2.7)                              |
|                      |            | Male           | 103            | 6 (5.8)                                    | 1 (1.0)                              |
|                      |            | All            | 222            | 14 (6.3)                                   | 4 (1.8)                              |
| Total                |            |                | 242            | 18 (7.4)                                   | 6 (2.5)                              |

# Table 1. Detected of Anaplasma phagocytophilum and Anaplasma platys in ticks by species, district and gender, Selenge province, Mongolia, 2013

closely related to the *Anaplasma phagocytophilum* detected in *Ixodes persulcatus* ticks from Novosibirsk (GenBank:HM366569.1) and from Sverdlovsk (GenBank:HM366567.1) in the Russian Federation and were genetically distinct from *Anaplasma phagocytophilum* agents found in Europe-I, Europe-II and USA groups (**Figure 1**).

# DISCUSSION

Discrepant infection of Anaplasma phagocytophilum in ticks has been observed around the world. In this study, both Anaplasma phagocytophilum and Anaplasma platys infection were detected in ticks from the forest area of Selenge province, Mongolia. For Ixodes persulcatus ticks the prevalence of Anaplasma phagocytophilum was 6.3%, similar to the 4.6% reported in a previous study from Inner Mongolia Autonomous Region and Heilongjiang Province, China.<sup>8</sup> Infection in female Ixodes persulcatus ticks was higher than in males. Anaplasma platys infection in Ixodes persulcatus ticks was 1.8%. For Dermacentor nuttalli ticks, Anaplasma phagocytophilum was detected in 20% and Anaplasma platys in 10%. This suggests that these tick species may play a role in the transmission of both Anaplasma phagocytophilum and Anaplasma platys from ticks to humans in nature.

The phylogenetic tree showed clustering within the Russian group most closely with other samples from the same tick species from the Russian Federation genetically distinct from agents found in and Ixodes ricinus ticks, ruminants, horses, humans and more. As Selenge province is located in the north part of Mongolia and borders the Russian Federation, it has a similar geographical topography and therefore this result is not surprising. Ixodes persulcatus is the vector of Anaplasma phagocytophilum in Asia, the Ural Mountains in the Russian Federation, Siberia, the Far East and in the Russian Baltic region.<sup>9</sup> Ixodes persulcatus is distributed within the north and north-eastern parts of Mongolia; Dermacentor nuttalli is more widely distributed throughout Mongolia.

To the author's knowledge, this study is the first description of *Anaplasma phagocytophilum* and *Anaplasma platys* in ticks in Mongolia and has both veterinary and public health significance given that these agents can cause both animal and human illness. As there is already serological evidence of human illness from *Anaplasma phagocytophilum* in Mongolia,<sup>6</sup> an understanding of the transmission mechanisms from tick to humans is required to develop prevention methods for HGA.

## Conflicts of interest

None declared.

## Funding

None.

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# Epidemiology and control of tuberculosis in the Western Pacific Region: analysis of 2012 case notification data

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Tuberculosis (TB) control in the World Health Organization (WHO) Western Pacific Region has seen substantial progress in the last decade, with a 33% reduction in prevalent TB cases since 2000. The burden remains immense, however, and national TB programmes must evolve and adapt to build upon these gains. Through routine surveillance, countries and areas in the Region reported 1.4 million TB cases in 2012. The case notification rate increased in the early 2000s, appears to have stabilized in recent years and is in decline for all forms and new smear-positive cases. The age and sex breakdown for smear-positive TB case rates by country shows generally higher rates with increased age and declining rates over time for all age groups. Treatment success remains high in the Region, with 15 countries reaching or maintaining an 85% success rate. HIV testing among TB patients has increased gradually along with a slow decline in the number of HIV-positive patients found.

The trend of TB notification is heavily influenced by programmatic improvements in many countries and rapidly changing demographics. It appears that cases are being found earlier as reflected in declining rates of smear-positive TB and steady rates of TB in all forms. WHO estimates depict a decline in TB incidence in the Region. HIV testing, while still low, has increased substantially in recent years, with essential TB/HIV services expanding in many countries.

TB surveillance data, within inherent limitations, is an important source of programmatic and epidemiological information. Careful interpretation of these findings can provide useful insight for programmatic decision-making.

ignificant progress has been made in tuberculosis (TB) control in the World Health Organization (WHO) Western Pacific Region especially in the past decade. The number of prevalent TB patients in the Region fell from 3.6 million in 2000 to 2.4 million in 2012.<sup>1</sup> During the same period, over 10 million patients were diagnosed and treated, and an estimated 800 000 deaths were averted.<sup>2</sup> According to the latest WHO estimates, the Region is on track for achieving the TB-related Millennium Development Goals (MDGs) and other international targets by 2015. However, with 1.4 million TB patients notified annually in the Region and several countries with a persistent substantial disease burden, TB control policies and strategies require continuous evolution to adopt new tools and approaches as well as to address emerging challenges faced by national TB control programmes. In light of the MDG target date approaching, WHO has embarked on an extensive consultative process of developing a new global TB strategy after 2015.<sup>3</sup> At this critical period of strategy renewal, a thorough analysis of surveillance

data provides valuable information on the current epidemiological situation, programmatic progress and future directions.

Throughout the year of 2014 and beyond, we plan to conduct a series of further regional analyses on various topics such as subnational data analysis and utilization, the situation of drug-resistant TB, contact investigation and other forms of TB screening activities to stimulate the utilization of surveillance data for informed programme decision-making.

# **METHODS**

# Data

Every year, 36 countries and areas in the Region are requested to report TB surveillance data to WHO using a standardized data collection form. Since 2009, a webbased online system has been used for data submission and validation. Collected data cover the following

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Submitted: 14 February 2014; Published: 24 March 2014; Erratum: 16 June 2014 Erratum: 16 June 2014 (Figure 5 graph corrected) doi: 10.5365/wpsar.2014.5.1.013

areas: TB case notifications and treatment outcomes. diagnostic and treatment services, drug management, surveillance and surveys of drug resistance, information on TB/HIV co-infection, infection control, engagement of all care providers and budgets and expenditures for TB control. The full description of methods is available in the Global Tuberculosis Report 2013 and the data sets are available from the WHO global TB database (www. who.int/tb/data). Case definitions for TB can be found in the 4th edition of the TB treatment guidelines.<sup>4</sup> In 2013, 30 countries and areas of the Western Pacific Region reported data representing more than 99.9% of the total population. This report described the epidemiological situation and progress in programmatic response with a focus on seven countries with a high burden of TB: Cambodia, China, the Lao People's Democratic Republic, Mongolia, Papua New Guinea, the Philippines and Viet Nam. (Globally, WHO designates 22 countries including Cambodia, China, the Philippines and Viet Nam with a high burden of TB. The other three countries - the Lao People's Democratic Republic, Mongolia and Papua New Guinea - are considered priority countries with a high burden of TB in the Western Pacific Region).

#### Analysis and reproducibility

Analysis was conducted by the statistical package R (R Core Team, 2013, Vienna, Austria, www.R-project. org). Due to calls for transparent and reproducible research,<sup>5,6</sup> we have published programme code to generate the entire contents of this article including all figures and tables by using R with the knitr package (Yihui Xie, 2013). Readers can request copy of the code and reproduce all figures and tables under an appropriate personal computing environment. For non-commercial purposes, readers may modify the code to produce figures and tables that are not presented in this article. For instance, readers may wish to produce tables and figures for countries or regions other than the WHO Western Pacific Region.

# RESULTS

# **Case notification**

In 2012, countries and areas in the Region reported 1 410 835 people with TB disease (**Table 1**), making up 23% of the global burden.<sup>1</sup> Of these cases, 97.5% (1 375 713) were new episodes of TB disease (either

new or relapse cases). Within the Region, China accounts for 64% (900 678) of the caseload, with the Philippines and Viet Nam following with 16% (230 162) and 7% (103 906), respectively. TB notification rates, expressed as cases per 100 000 population, vary substantially in the Region, with the highest rates found in Kiribati, Papua New Guinea, the Marshall Islands, Cambodia and the Philippines (343, 287, 276, 270 and 224 per 100 000 population, respectively [**Figure 1**, **Table 1**]).

Between 2002 and 2007, case notification rates in the Region increased from 47 to 77 per 100 000 population in all forms of TB and from 22 to 38 per 100 000 population in new smear-positive TB cases. After 2005, the case notification rates for all forms of TB stabilized, and new smear-positive cases seem to have started to decrease (**Figure 2**).

#### Distribution by age and sex

**Figure 3** shows age- and sex-specific case notification rates of new smear-positive cases for the seven countries with a high burden of TB in the Region (note that the scale of the vertical axis is different for each country). Many countries follow a typical pattern for cross-sectional observations with increasing notification rates towards older populations except Mongolia and Papua New Guinea. In general, males are more affected than females, with male-to-female TB ratios 3:1 in Viet Nam.

**Figure 4** shows trends of notification rates of new smear-positive cases of age- and sex-specific groups in the seven countries with a high burden of TB from 2000 to 2012. Some countries such as Cambodia, China and Viet Nam demonstrated a declining trend of case notification for almost all age- and sex- groups, while others showed a less apparent trend. Papua New Guinea showed a sharply increasing trend.

#### **Treatment outcomes**

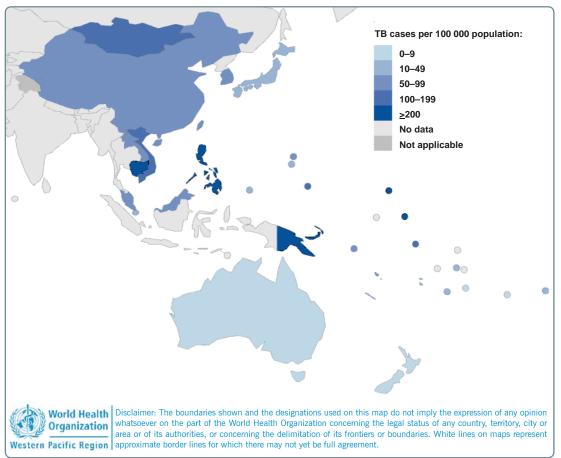
The Region continued observing treatment success rates beyond the target of 85% (Figure 5), and the rate has been at 85% or higher over the past several years. Across the Region, 15 countries and areas reached or maintained the 85% treatment success target. Among the countries with a high burden of TB,

|  |                   | Total                        |                   |                   |                   | Re-treatment cases  |           |                                  |       |         |                                      |                        |
|--|-------------------|------------------------------|-------------------|-------------------|-------------------|---------------------|-----------|----------------------------------|-------|---------|--------------------------------------|------------------------|
| Countries and areas                    | Total<br>notified | notified<br>(per<br>100 000) | Smear<br>positive | Smear<br>negative | Smear<br>not done | Extra-<br>pulmonary | Case type | Pulmonary<br>laborat<br>confirme | ory-  | Relapse | Re-treatment<br>excluding<br>relapse | New<br>and<br>relapse* |
| American<br>Samoa                      |                   |                              |                   |                   |                   |                     |           |                                  | _     |         |                                      |                        |
| Australia                              | 1 325             | 6                            | 290               | 330               | 78                | 498                 | 63        | 667                              | (96)  | 26      | 20                                   | 1 305                  |
| Brunei<br>Darussalam                   | 243               | 59                           | 119               | 51                | 28                | 31                  | 0         | 166                              | (84)  | 14      | 0                                    | 243                    |
| Cambodia                               | 40 258            | 270                          | 14 838            | 8 509             | 0                 | 15 290              | 0         | 14 838                           | (64)  | 446     | 73                                   | 40 185                 |
| China                                  | 900 678           | 65                           | 316 332           | 533 977           | 2 073             | 6 479               | 0         | 316 332                          | (37)  | 31 784  | 10 033                               | 890 645                |
| Hong Kong<br>(China)                   | 4 969             | 67                           | 1 463             | 2 004             | 202               | 817                 | 0         | 2 704                            | (74)  | 323     | 160                                  | 4 809                  |
| Macao (China)                          | 406               | 73                           | 156               | 137               | 2                 | 31                  | 0         | 241                              | (82)  | 26      | 2                                    | 404                    |
| Cook Islands                           | 1                 | 5                            | 0                 | 0                 | 0                 | 0                   | 0         | 0                                | -     | 1       | 0                                    | 1                      |
| Fiji                                   | 218               | 24                           | 111               | 54                | 0                 | 40                  | 0         | 165                              | (100) | 5       | 8                                    | 210                    |
| French<br>Polynesia                    | 50                | 18                           | 26                | 10                | 0                 | 8                   | 0         | 33                               | (92)  | 6       | 0                                    | 50                     |
| Guam                                   | 68                | 42                           | 23                | 23                | 14                | 8                   | 0         | 31                               | (52)  | 0       | 0                                    | 68                     |
| Japan                                  | 21 283            | 16                           | 7 663             | 7 454             | 221               | 4 609               | 0         | 13 013                           | (85)  | 910     | 426                                  | 20 857                 |
| Kiribati                               | 348               | 343                          | 134               | 122               | 0                 | 73                  | 9         | 134                              | (52)  | 8       | 2                                    | 346                    |
| Lao People's<br>Democratic<br>Republic | 4 156             | 62                           | 3 062             | 484               |                   | 351                 |           | 3 062                            | (86)  | 168     | 38                                   | 4 118                  |
| Malaysia                               | 22 710            | 75                           | 13 311            | 4 941             | 52                | 2 945               | 0         | 13 311                           | (73)  | 602     | 859                                  | 21 851                 |
| Marshall Islands                       | 147               | 276                          | 54                | 39                | 14                | 29                  | 0         | 54                               | (50)  | 4       |                                      | 145                    |
| Micronesia,<br>Federated<br>States of  | 146               | 139                          | 43                | 75                | 2                 | 22                  | 0         | 58                               | (48)  | 2       | 2                                    | 144                    |
| Mongolia                               | 4 453             | 148                          | 1 716             | 617               | 0                 | 1 611               | 0         | 1 716                            | (74)  | 184     | 325                                  | 4 128                  |
| Nauru                                  |                   |                              |                   |                   |                   |                     |           |                                  | _     |         |                                      |                        |
| New Caledonia                          | 38                | 15                           | 13                | 11                | 0                 | 12                  | 1         | 24                               | (100) | 1       | 0                                    | 38                     |
| New Zealand                            | 297               | 7                            | 68                | 88                | 11                | 112                 | 3         | 143                              | (86)  | 11      | 4                                    | 293                    |
| Niue                                   | 0                 | 0                            | 0                 | 0                 | 0                 | 0                   | 0         | 0                                | -     | 0       | 0                                    | C                      |
| Northern<br>Mariana Islands            | 34                | 60                           | 10                | 17                | 0                 | 4                   | 1         | 15                               | (56)  | 0       | 2                                    | 32                     |
| Palau                                  | 4                 | 19                           | 3                 | 1                 | 0                 | 0                   | 0         | 3                                | (75)  | 0       | 0                                    | 2                      |
| Papua New<br>Guinea                    | 22 488            | 287                          | 2 862             | 2 046             | 7 149             | 8 277               | 0         | 2 862                            | (24)  | 223     | 1 931                                | 20 557                 |
| Philippines                            | 230 162           | 224                          | 94 006            | 115 263           | 0                 | 3 274               | 0         | 94 006                           | (45)  | 4 084   | 13 535                               | 216 627                |
| Republic of<br>Korea                   | 49 532            | 89                           | 12 137            | 15 622            | 3 316             | 8 470               | 0         | 28 397                           | (91)  | 4 157   | 5 830                                | 43 702                 |
| Samoa                                  | 22                | 12                           | 15                | 4                 | 0                 | 3                   | 0         | 19                               | (100) | 0       | 0                                    | 22                     |
| Singapore                              | 2 364             | 43                           | 678               | 1 093             | 126               | 306                 | 0         | 1 206                            | (64)  | 98      | 63                                   | 2 301                  |
| Solomon Islands                        | 372               | 66                           | 157               | 87                | 0                 | 112                 | 0         | 157                              | (64)  | 5       | 11                                   | 361                    |
| Tokelau                                |                   |                              |                   |                   |                   |                     |           |                                  | _     |         |                                      |                        |
| Tonga                                  | 11                | 10                           | 9                 | 1                 | 0                 | 1                   | 0         | 10                               | (100) | 0       | 0                                    | 11                     |
| Tuvalu                                 | 20                | 193                          | 8                 | 2                 | 0                 | 9                   | 0         | 9                                | (90)  | 0       | 1                                    | 19                     |
| Vanuatu                                | 126               | 51                           | 51                | 22                | 0                 | 51                  | 0         | 73                               | (100) | 1       | 1                                    | 125                    |
| Viet Nam                               | 103 906           | 112                          | 51 033            | 21 706            |                   | 18 904              | 3 210     | 51 033                           | (70)  | 7 259   | 1 794                                | 102 112                |
| Wallis and<br>Futuna Islands           |                   |                              |                   |                   |                   |                     |           |                                  | _     |         |                                      |                        |
| Western Pacific<br>Region              | 1 410 835         | 75                           | 520 391           | 714 790           | 13 288            | 72 377              | 3 287     | 544 482                          | (44)  | 50 348  | 35 122                               | 1 375 713              |

# Table 1. TB case notification from countries and areas of the Western Pacific Region, 2012

Blank cells indicate data not reported; "-" indicates values that cannot be calculated. \* New and relapse – includes cases for which the treatment history is unknown. Note: Data reported as of 1 October 2013.

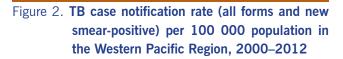


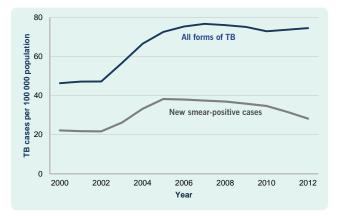


the treatment success rate was highest in China (96%), followed by Cambodia (94%), Viet Nam (93%), the Lao People's Democratic Republic (92%), the Philippines (90%) and Mongolia (85%). The treatment success rate of Papua New Guinea was the lowest at 69%, with approximately a quarter of the 2011 cohort either defaulted or not evaluated.

# TB/HIV co-infection and collaborative activities

There has been some progress in reporting of information on TB/HIV co-infection and collaborative activities in the last several years. **Figure 6** summarizes four basic indicators (HIV testing, HIV positivity rate, co-trimoxazole preventive therapy [CPT] coverage and antiretroviral therapy [ART] coverage) for the seven countries with a high burden of TB. Cambodia reported the most comprehensive data completeness and programmatic progress. The coverage of HIV testing, CPT and ART progressively increased with a steady decrease in the proportion of HIV-positive individuals among TB patients.





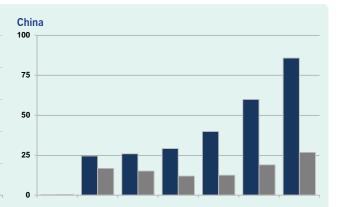
# DISCUSSION

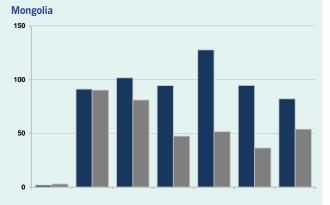
Overall, in 2012, countries and areas of the Western Pacific Region reported 1.4 million TB cases (all forms) and a case notification rate of 75 per 100 000 population, a level similar to the past several years.

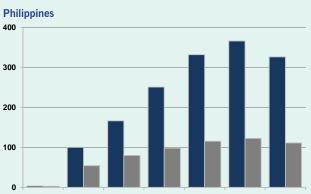
Cambodia

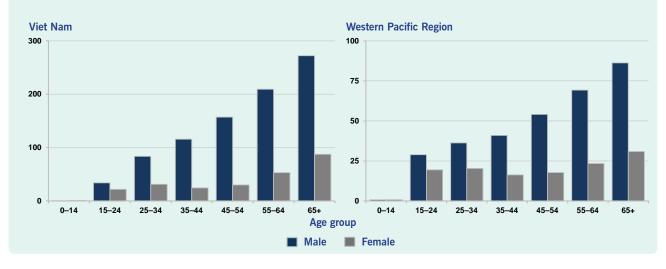


Lao People's Democratic Republic New smear-positive cases per 100 000 population Papua New Guinea 









# Male Female Cambodia 150 100 China Lao People's Democratic Republic 100 150 New smear-positive cases per 100 000 population Aoneolia 0–14 15–24 25–34 35-44 45-54 Papua New Guinea 55-64 65+ 500 400 Philippines 300 200 20 100 100 500 50 40 Viet Nam 300 30 200 20 100 10 150 150 Western Pacific Region 100 2008 2009 2010 2011 2012 2003 2004 2005 2007 2010 2011 2012 2002 2006 Year



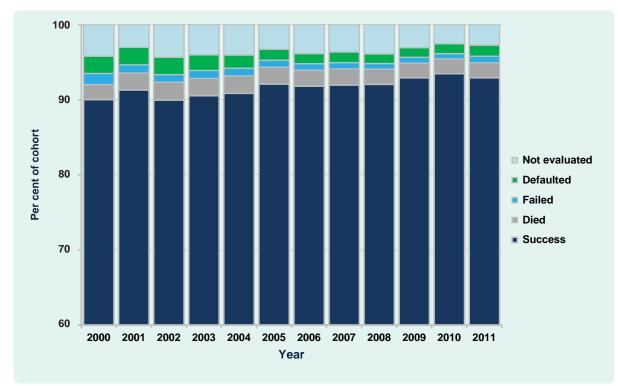


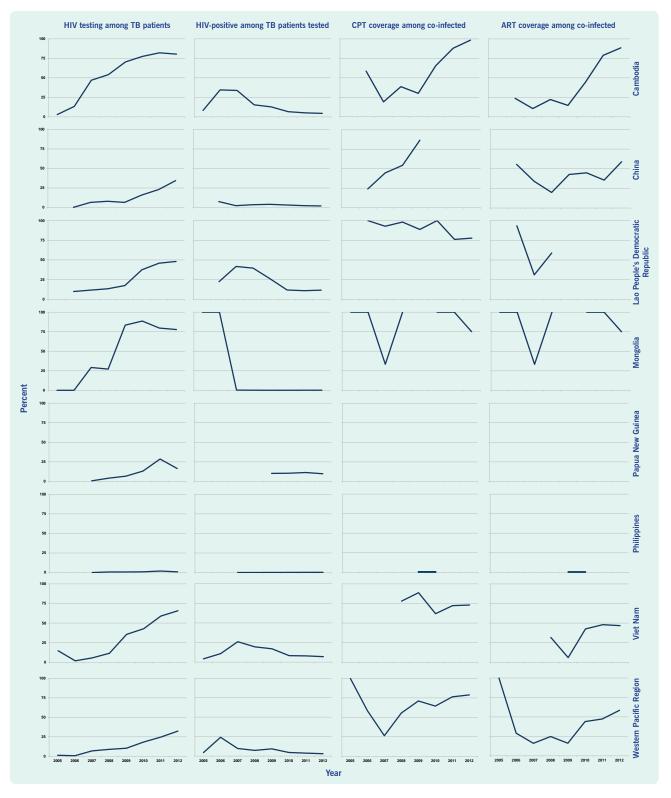
Figure 5. Trend of treatment outcome expressed as a proportion among new pulmonary smear-positive cases in the Western Pacific Region, 2000–2011

It has been known that the rapid increase in case notification between 2002 and 2007 was due to several positive programmatic developments in many countries in the Region such as completion and consolidation of the WHO directly observed treatment, short-course strategy expansion; improvement in case reporting, including electronic reporting systems; and efforts to engage all health-care providers.<sup>7</sup> Particularly, renewal of infectious disease-related legislation and the establishment of an Internet-based disease notification system in China made a substantial contribution to the progress.<sup>8</sup>

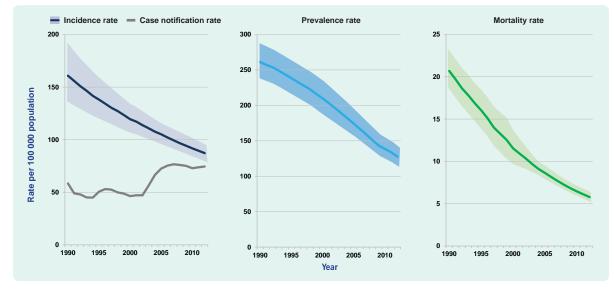
Although case notification for all forms of TB appears to have been flat since 2007, it is important to note that the new smear-positive case notification rates demonstrate a clear declining trend (**Figure 2**). A possible interpretation is that the true TB incidence has been declining while overall case detection has been static because intensified programmatic efforts by national TB programmes for early and increased case detection include smear-negative and extrapulmonary TB. The latest WHO estimates support this explanation, with estimated incidence rates showing a consistent, rapidly declining trend (**Figure 7**).<sup>1</sup>

In any country where a rapid demographic change is under way, overall notification rates may not reflect a true disease trend in the communities. For instance, an overall case notification trend may appear to be stable because decreasing incidences can be cancelled out by a rapidly increasing proportion of an older population. For this reason, the examination of age- and sex- specific case notification rates is more informative and provides insights for understanding the underlying epidemiological process in a given setting.

The typical pattern of linear increase of notification towards the older populations (such as shown in some countries in **Figure 3**) has been explained as a widely observed phenomena under a stable TB control situation,<sup>9</sup> reflecting a high annual risk of TB infection in the past when the older population was young. Atypical patterns shown for Papua New Guinea and Mongolia, particularly relatively high notification rates among young and female groups, warrant further investigation. Time trend analysis for age- and sex- notification rates (**Figure 4**) is useful to detect any specific subgroups among which TB transmission and/or disease progression is particularly active.



# Figure 6. Progress in TB/HIV activities in seven countries in the Western Pacific Region with a high burden of TB, 2005–2012



# Figure 7. TB case notification rate, estimated incidence, prevalence and mortality per 100 000 population in the Western Pacific Region, 1990–2012

Note: Shaded parts represent uncertainty bands.

One of the critical shortcomings of these analyses is a gross lack of morbidity information among small children because the data are limited to smear-positive cases only. Since the 2006 revision of WHO recording and reporting forms,<sup>10</sup> the number of countries reporting age- and sex-disaggregated data for smear-negative and extrapulmonary cases has been increasing and will enable a better assessment of the TB burden among children in future analysis.

HIV infection fuels the TB epidemic, particularly in countries and areas with a high burden of TB. The overall percentage of TB patients tested for HIV in the Region still remains low. However, the figure has substantially increased in the last several years, particularly in Cambodia, Viet Nam and the Lao People's Democratic Republic. Essential services such as co-trimoxazole prophylaxis and isoniazid preventive therapy have also expanded in many countries in the Region.

This report provides a snapshot of the epidemiological and programmatic situation of TB in the Western Pacific Region based on case notification data in 2012. As for any disease surveillance system, the analysis of surveillance data has inherent limitations. TB surveillance covers populations served by care providers linked with the national TB programme. Ideally

this would include all known cases in the country; in practice the proportion of cases diagnosed outside of the TB programme and included in national reporting varies depending on the legal framework in the country. The WHO TB Impact Measurement Task Force recommends that countries continuously improve surveillance systems until reported cases can be considered a reliable proxy for incidence.<sup>11</sup> A careful assessment is needed of programmatic progress in the country and the quality of surveillance data when interpreting these findings.

TB surveillance continues to be an important source of information for assessing the situation and measuring the progress for decision-making. The WHO Regional Office for the Western Pacific will continue to conduct regional analysis on various topics related to TB epidemiology and programmatic progress, as well as provide support to countries to conduct epidemiological and programmatic assessment at national and subnational levels.

# Conflicts of interest

None declared.

### Funding

None.

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- 11. TB Impact Measurement. Geneva, World Health Organization, 2009.

# Western Pacific Surveillance and Response Instructions to Authors

# **ABOUT WPSAR**

The aims of WPSAR are:

- 1. to provide an open access journal to publish articles on the surveillance of and response to public health events and emergencies in the WHO Western Pacific Region and in areas with relevance to the Western Pacific Region; and
- to build capacity in communicating epidemiological and operational research within the WHO Western Pacific Region.

Our objectives are:

- to provide a platform for people working in surveillance and response in the Western Pacific Region to share their scientific and operational findings;
- 2. to publish a broad range of articles not limited to conventional research articles:
  - to disseminate short reports on outbreak investigations;
  - to publish analyses of surveillance data on communicable diseases;
  - to encourage the publication of evaluations of new and existing surveillance systems;
  - to promote the use of risk assessment for public health by facilitating risk assessment articles;
  - to support preparedness and response to public health events and emergencies through the dissemination of lessons learnt from such events; and
- to build capacity in communicating epidemiological and operational findings in the Western Pacific Region through pre-submission assistance.

### Scope

WPSAR covers all activities related to the surveillance of and response to public health events and emergencies, with a focus on topics that are relevant to the Western Pacific Region. Public health events may be acute or ongoing and can fall under any of the following areas: communicable diseases, natural disasters, food safety, bioterrorism, and chemical and radiological events. Other events and topics may also be considered. Response activities include those for acute events, e.g. responding to natural disasters, or for response to cases or epidemics of disease.

### Why publish in WPSAR?

WPSAR is not limited to conventional research. It publishes a broad range of articles, including short outbreak investigation reports, lessons from the field, analyses of surveillance data, evaluations of surveillance systems and risk assessments for public health events. There are limited opportunities to publish these types of articles in other journals. We also accept the more traditional original research, perspectives and case reports/case series articles.

WPSAR is an open access journal, meaning it is free of charge for both readers and authors. It is also a continuous publication, which means articles are published as soon as they have completed the review and editing process.

WPSAR accepts all articles that fit the scope of the journal and that meet the minimum publication standards. We are especially interested in field epidemiology and operational research. WPSAR also aims to build capacity in scientific writing and encourages submissions from authors with little or no experience in publishing in peer-reviewed journals. The Coordinating Editor often works with new authors on their submissions to ensure that articles fit the scope of WPSAR and meet the minimum standards for publication.

# INSTRUCTIONS TO AUTHORS FOR ARTICLE WRITING AND SUBMISSION

WPSAR follows the guidelines of the *Uniform Requirements for Articles Submitted to Biomedical Journals by the International Committee for Medical Journal Editors* (ICMJE).

#### **Formatting guidelines**

Please submit your article in a Microsoft® Office Word file or a compatible file in English. Double-spaced, 12-point Arial font should be used to format your article. Please remove all automatic formatting including automatic numbering and referencing before submitting.

The format of the article will depend on the article type. Please see below for specific instructions per article type.

## **Outbreak Investigation Report**

A short article describing a field or outbreak investigation including how it was detected, investigated and controlled. Rapid risk assessments undertaken during these investigations are also encouraged. These articles may be considered for rapid publication.

- Structured article with an abstract of  $\leq 250$  words and sections for introduction, methods, results and discussion
- Structured abstract with sections for objective, methods, results and discussion
- Word limit:  $\leq 1500$  words
- $\leq 15$  references
- ≤ 2 figures/graphs/pictures

More comprehensive investigations can be submitted as Original Research.

### Surveillance Report

A summary and interpretation of surveillance data over a given period of time. A description of the surveillance system and the limitations of the data collected must be included.

- Unstructured abstract of  $\leq 250$  words
- Word limit:  $\leq$  2000 words
- $\leq 15$  references
- ≤ 10 figures/graphs/pictures

### Surveillance System Implementation/Evaluation

An article describing the implementation of a new surveillance system or an evaluation of an existing surveillance system used to detect public health events.

- Unstructured abstract of ≤ 250 words
- Word limit:  $\leq$  2000 words
- $\leq 15$  references
- ≤ 3 figures/graphs/pictures

#### **Risk Assessments**

An article detailing a risk assessment of a public health threat or event.

- Structured article with an abstract ≤ 250 words and sections for introduction (including risk question/s), risk assessment methodology, results, discussion and recommendations
- Structured abstract with objectives, method, results and discussion
- The results should include an assessment and/or characterization of the hazard, exposure and context, as well as the level of risk or risk characterization. The limitations must also be included. Risk management may be included in the discussion.
- Word limit:  $\leq$  3000 words
- $\leq$  30 references
- ≤ 3 figures/graphs/pictures

#### **Original Research**

Original research articles may include epidemiological studies including outbreak investigations.

- Structured article with an abstract of ≤ 250 words and sections for introduction, methods, results and discussion
- Structured abstract with objective, methods, results and discussion
- Word limit:  $\leq$  3000 words
- $\leq$  40 references
- ≤ 5 figures/graphs/pictures

#### Lessons from the Field

An article describing a problem faced in field epidemiology or during a public health event and the experience in trying to overcome the problem.

- Structured article with an abstract ≤ 250 words and sections for problem, context, action, lesson(s) learnt or outcome and discussion
- Structured abstract with the headings of problem, context, action, lesson(s) learnt and discussion
- Word limit:  $\leq 2000$  words
- ≤ 15 references
- ≤ 3 figures/graphs/pictures

#### Perspectives

An unstructured article discussing an issue regarding the surveillance of and response to public health events. The scope of the discussion must be clearly defined.

- Word limit:  $\leq 1000$  words
- $\leq 10$  references
- ≤ 1 illustration

#### Case Report or Case Series

An unstructured article describing an unusual case or series of cases of public health significance. Subheadings may be used to increase the readability of the article.

- Unstructured abstract of ≤ 250 words
- Word limit:  $\leq 2000$  words
- $\leq 15$  references
- ≤ 3 figures/graphs/pictures

## Regional Analysis

An article providing an analysis of a topic for the Western Pacific Region, typically authored by WHO staff as part of their routine work on behalf of Member States. Regional Analyses do not undergo peer review.

## *Letter to the Editor*

A letter commenting on a previously published article OR a letter commenting on the theme of the issue. Letters do not undergo peer review.

- Word limit:  $\leq$  500 words
- ≤ 5 references
- ≤ 1 illustration

#### News, Meeting and Conference Reports

News items and meeting and conference reports do not undergo peer review. Please contact the Coordinating Editor at WPSAR@wpro.who.int if you intend on submitting such an article.

#### Illustrations

Refer to the article type for the limit on illustrations (figures/graphs/ pictures). Please insert all illustrations at the end of the article with titles. Each illustration must be referred to in the text and must be understood on its own. Use Microsoft® Office Excel for graphs and Microsoft® Office Word for tables and diagrams. Additionally, please provide a Microsoft® Office Excel spreadsheet of the data used to create a graph. Footnotes should be placed under the illustration and should use the following symbols in superscript format: \*, †, ‡, §,  $\|$ , \*\*, ††, etc.

#### References

Reference the most recent and relevant publications. Please use the Vancouver referencing style with in-text citations and a bibliography at the end of the text. Sample references can be viewed on the National Institutes of Health website.

Placethe bibliography at the end of the article text and not as footnotes. Write journal names in full. Use superscript sequential numbering for citing references in the text. Place the number after any punctuation. For example:

These results are consistent with the original study.<sup>11</sup>

Reference personal communication in the text only and include the person's full name and institution.

Caution should be used in referencing websites; it should be done only when their content has been substantially described in the article.

#### Peer review process

Every article is initially screened by the Editorial Team to ensure it fits the scope of the journal. All articles, with the exception of regional analyses, letters to the editor, news items and meeting and conference reports, then undergo external peer review by two reviewers. This blind peer review process ensures that the reviewer does not know the identity of the author(s) and the author(s) do not know the identity of the reviewer. Significant effort is made to make this process timely, but since it relies on the availability and cooperation of persons external to the journal, it can take considerable time.

Upon receipt of the reviews, the Coordinating Editor assesses the comments and recommendations made by the reviewers, and then decides on the outcome of the peer review process. One of four options will be chosen: accept submission, accept with revisions, submit for review, or decline submission. The corresponding author will be advised of this outcome.

If the article has been accepted or accepted with revisions are required, you will be invited to revise your article according to the reviewer comments. A separate MS Word document outlining how you addressed each of the reviewer comments is also required. You must indicate the page and paragraph numbers where the changes were made and should provide reasons for not making a suggested change. Both the changes and reasons will be assessed against the reviewer comments by the Coordinating Editor and may require further clarification from the authors. Once all comments have been adequately addressed, the article will commence the publication process.

If the outcome of the review process is "submit for review", then the same process is followed. However, the resubmitted article and responses to the reviewer comments are sent back to the original reviewers for another round of peer review. You will be asked to respond to a second round of reviewer comments, which will again be assessed by the Coordinating Editor. Once both sets of reviewer comments have been adequately addressed, the article will commence the publication process.

The publication process comprises rigorous editing for content and style by an external technical editor, followed by layout and proofreading. Authors may be asked to provide further information or clarifications during these stages. An article is not formally accepted for publication until these stages have been completed and approval has been granted by the Editorial Team. The authors will also have an opportunity to approve the final proof prior to publication on the WPSAR website. The article will be batched with others in the next quarterly issue.

## Authorship

As per the International Committee of Medical Journal Editors (ICMJE), all authors should have contributed significantly to the article through one or more of the following in each category A, B and C:

#### Α

- Study design
- Data collection
- Data analysis
- Data interpretation

#### В

- Drafting the article
- Critically revising the article

### С

• Final approval of the article for submission

Any other contributors may be listed in the Acknowledgements section.

### Acknowledgements

Contributors who do not fulfil the authorship requirements may be acknowledged. Permission from all contributors in the acknowledgement section should be sought. We assume that permission has been granted and will not follow up with the authors to confirm.

### **Ethics and permissions**

It is the responsibility of authors to gain appropriate ethics approval for their work. A statement of ethics approval obtained or an explanation of why ethics approval was not required should be included for all articles during the submission process.

### License for publication

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## **Conflicts of interest**

A conflict of interest is defined by ICMJE as "when an author or author's institution, reviewer, or editor has financial or personal relationships that inappropriately influence (bias) his or her actions". Conflicts of interest may be financial, institutional, research or personal. A relationship does not always represent a conflict of interest and does not necessarily preclude publication in WPSAR. All authors and reviewers will be required to state any potential conflicts of interest, which will be assessed by the Editorial Team.

### Funding

Authors will be required to state the sources of funding for their work.

#### Photographs for cover

If authors have taken photographs that are relevant to their article, they may be submitted for consideration for publication on the cover of the issue. Submission of a photograph does not guarantee its publication.

#### Language

Articles should be written in English. Authors who require assistance with preparing their articles in English should contact WPSAR at WPSAR@wpro.who.int. Once published, all abstracts and most articles are translated into Chinese.

#### Article submission process

Submit articles to the Coordinating Editor through the online journal management system on the WPSAR website. When submitting the article, you will be requested to provide the following:

- a cover letter describing the article and why it should be published;
- a title page with:
- the article title,
- a short title,
- a brief description of the article of  $\leq$  50 words,
- $\leq 7$  keywords,
- full names of all authors and institutions,
- full contact details of the corresponding author,
- data in an MS Excel spreadsheet for any graphs
- names and e-mail addresses of two suggested reviewers (optional but recommended);
- acknowledgements, conflicts of interest, ethics statement and funding information (attached as a separate file to ensure a blind review);
- an MS Word file or equivalent of the article; and
- a scanned copy of the WPSAR licence for publication signed by all authors.

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### Corrections

If authors of a published article become aware of any errors with the article, they should contact the Coordinating Editor at WPSAR@wpro.who.int. Corrections will be published online.





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