Western Pacific Surveillance and Response

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

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RESURGENCE OF DENGUE

Globally, the challenge posed by dengue has escalated at an astonishing rate in the last three decades, with no sign of abating. It is estimated that dengue affects at least 50 million – 100 million people every year. With more than 120 dengue-endemic countries, 3.6 billion people are at risk of infection. More than 70% of those at risk reside in the Asia Pacific region, making this region an epicentre of dengue activity.

In addition to making a comeback in places such as the Americas and Singapore, where dengue was previously successfully controlled for decades, the virus has also breached the subtropical-temperate barrier as it claims new territories. In the last decade, dengue transmission has extended its reach into places as far north as Nepal, Ningbo in China and France, and as far south as Bueno Aires in Argentina. The Pacific islands, with much lower population densities, have also not been spared, with increasing dengue outbreaks since the 1970s.

The direct economic and social impact of dengue on dengue-endemic regions is high, and the burden in other aspects such as the security of blood supplies is increasingly being recognized. Dengue's threat to travellers has also been systematically demonstrated by a 2008 study on 6957 travellers who returned ill and sought treatment from EuroTravNet centres. Of those travellers, 1.9% were diagnosed with dengue, and one of the three deaths reported was due to dengue shock syndrome.

FACTORS THAT CONTRIBUTED TO THE CHALLENGE

Key contributing factors to the worldwide resurgence of dengue in the last few decades include the rise in number and size of densely populated urban cities that are conducive for the spread of the disease and the adaptation and proliferation of dengue vectors, particularly the primary carrier of dengue virus, Aedes aegypti. In the last three decades, the number of people living in cities around the world has doubled from 1.7 billion to 3.5 billion. The number is expected to rise to 5 billion by 2030, and most of this is projected to occur in Asia. Furthermore, increased global travel has facilitated the spread of the virus. The resultant increase in transmission of the viruses has brought about genetic expansion of virus, providing ample opportunities for successful selections of viral variants of high epidemic potential or virulence as suggested by molecular epidemiological studies on Cuba and Puerto Rico. The geographical expansion of the vector, Aedes aegypti, is also well demonstrated by its recent invasion or reinvasion into temperate regions, such as Nepal and Bueno Aires in Argentina, and into rural areas in Indonesia and Cambodia. The vectorial role of Aedes albopictus, a mosquito that has successfully established its territory from South-East Asia to northern Asia (Japan and China), the Americas and Europe, has also been clearly revealed by dengue outbreaks in many places such as Hawaii, Hong Kong (China) and Ningbo, China.

Dengue vaccine is not available, and its development is hindered by the lack of suitable animal models and the requirement for a robust tetravalent vaccine that covers all four serotypes of dengue. With only one vaccine in the third phase of clinical trial, it is estimated that a dengue vaccine will not be available for at least the next seven years. Vector control remains the key strategy in dengue prevention and control. Unfortunately, the extensive and often indiscriminate use of insecticides has resulted in a global pandemic of insecticide resistance.

STRATEGY

The urban and peri-domestic habitats of Aedes aegypti offer an opportunity to suppress the vector population through source reduction, careful environment...
management and urban planning to deprive the Aedes mosquitoes of stagnant water for breeding. The success of this strategy has been demonstrated in the Americas and in Singapore in the 1950s and 1960s; Aedes aegypti was either eradicated or suppressed to a population that eliminated dengue or moderated dengue transmission to low endemicity. However, the recent resurgence has shown the limitation of the traditional strategy. It calls for more innovations and a better framework for surveillance and control.

INTER-EPIDEMIC SURVEILLANCE AND CONTROL

To battle with a complex disease like dengue, four cornerstones are required to support a robust surveillance system: human cases, virus, entomological and ecological surveillance. Today’s better understanding of the epidemiology of dengue, coupled with technologies such as geographical information systems, polymerase chain reaction, rapid antigen test kits, sequencing and bioinformatics, have offered us an opportunity to take a holistic approach in our undertaking to suppress the resurgence of dengue.

UNITED IN TACKLING EPIDEMIC DENGUE

Dengue does not respect political boundaries; neither does it respect divisions of government agencies or communities. Formation of linkages among those entities is critical for success of control programmes and is consistent with the Integrated Vector Management strategy promoted by the World Health Organization (WHO). Intersectoral linkage is critical to ensure that the activities of other sectors such as urban development, agriculture or water resources do not compromise any vector control programme; instead, vector control should be an agenda of each sector. The complexity of the disease also requires concerted effort among laboratory personnel of multi-disciplines, field officers, policy-makers and the community. The stakeholders are many in the control of dengue. An effective programme requires effective communications among various stakeholders, with elements of feedback and data sharing. The chain of events and measures that support surveillance, clinical management and control is not unlike a chain of links – the chain is only as strong as its weakest link.

Recognizing the importance of cross border-linkages, the Asia Pacific Dengue Partnership was formed in March 2006 to support and facilitate effective implementation of a prevention and control strategy so as to reverse the rising trend of dengue in the Asia Pacific region. Under the Partnership, Member States of the Western Pacific and South-East Asia Regions joined efforts with WHO in formulating the 2008–2015 Bi-Regional Dengue Strategic Plan, which was subsequently endorsed by the Regional Committees in September 2008, to be employed as a road map for national plans. Several activities, including the Asia Pacific Dengue Programme Managers’ Meeting and Asia Pacific Dengue Workshops, have been conducted to support the Plan in knowledge exchange and capacity-building. The recently updated Asia Pacific Strategy for Emerging Diseases, known as APSED (2010), provides a common strategic framework for countries and partners to work collectively to strengthen the national and regional disease surveillance and response systems and capacities, including dengue surveillance, outbreak response, clinical management and risk communications.

Despite progress made, many challenges remain, including: standardization of classification of dengue, enhancement of cases, vector and virus surveillance, limited resources and infrastructure for surveillance and control, quality of diagnostics, limited access to good clinical care, need for more advance entomological tools and the limited research that are eventually translated to disease prevention and management. Dengue is a serious problem that is already challenging us, and it threatens to be more aggressive. More support, attention, action and synergistic collaboration among all stakeholders are urgently needed to enhance the current systems.

Reference:


Dengue is an emerging vectorborne infectious disease that is a major public health concern in the Asia Pacific region. Official dengue surveillance data for 2010 provided by ministries of health were summarized as part of routine activities of the World Health Organization Regional Office for the Western Pacific. Based on reported data, dengue has continued to show an increasing trend in the Western Pacific Region. In 2010, countries and areas reported a total of 353,907 dengue cases, of which 1073 died, for a case fatality ratio of 0.30%. More than 1000 cases were reported each from Australia (North Queensland), Cambodia, the Lao People’s Democratic Republic, Malaysia, the Philippines, Singapore and Viet Nam. With the exception of Australia, the number of reported cases in 2010 was greater than that reported in 2009 for these countries. The elevated number of cases reported in 2010 in some countries, such as the Philippines, is likely due to several factors, such as enhanced reporting and continued epidemic activity. However, increases in reported number of cases in other areas, such as Singapore and Malaysia, appear to indicate sustained epidemic activity in those countries. The continued epidemic dengue activity in the Region highlights the need for timely and routine regional sharing of information.

In 2009, 14 Pacific island countries and areas reported dengue outbreaks, and five reported high dengue incidence: American Samoa (644/100,000 population), Cook Islands (1,090/100,000 population), French Polynesia (922/100,000 population), New Caledonia (3,443/100,000 population) and Tonga (263/100,000 population). While dengue surveillance is not conducted in Papua New Guinea, circulation of dengue virus there is well known by the importation of cases into Australia.3,4

Through this epidemiologic update, the WHO Regional Office for the Western Pacific aims to communicate the latest regional dengue situation. This report is the first of its kind and the goal is to continue such communication on a routine basis and encourage the countries and areas in the Western Pacific Region to maintain their surveillance and reporting activities.

METHODS
This report provides a descriptive summary of the regional dengue situation for 2010 based on data derived from indicator-based surveillance systems in the Region. Particular focus is given to dengue-endemic countries where dengue surveillance systems exist (i.e. Cambodia, the Lao People’s Democratic Republic, Malaysia, the Philippines, Singapore and Viet Nam);
Australia is also included as periodic dengue outbreaks occur in North Queensland. WHO Regional Office for the Western Pacific, with the assistance of WHO country offices, obtains these data on a biweekly basis from ministries of health, and collection of such information, along with periodic risk assessment, are routine activities of the Regional Office. The timeliness of reporting and completeness of reporting sites and surveillance data vary by country, and the latest information available is presented. The Regional Office also feeds back these data to countries and areas on a biweekly basis through http://www.wpro.who.int/health_topics/dengue.

RESULTS

Dengue in the Western Pacific Region

In 2010, Western Pacific Region countries and areas reported a total of 353,907 cases, of which 1,073 people died, for a case fatality ratio (CFR) of 0.30%. While incidence of dengue was largest in the Lao People’s Democratic Republic, the total numbers of cases and deaths reported were largest for the Philippines (Table 1). Summarization and reporting of the 2010 dengue data from the Pacific subregion are ongoing, but more than 100 cases were reported each from French Polynesia, New Caledonia and Vanuatu (Table 1). While dengue is not endemic in New Zealand, 51 cases were reported in 2010; all cases had overseas exposures with 12% of cases associated with travel to Vanuatu. Detailed information for countries with more than 1000 reported cases (Australia [North Queensland], Cambodia, the Lao People’s Democratic Republic, Malaysia, the Philippines, Singapore and Viet Nam) is presented below. With the exception of Australia, the number of reported cases in 2010 was greater than that reported in 2009 for these countries (Table 2).

Asia Subregion

Cambodia

Under the National Dengue Control Programme, suspected or probable dengue cases are reported through seven sentinel sites and other non-sentinel sites. In 2010, Cambodia reported 12,500 cases (38 fatal), with a peak (n = 835 cases) during week 31 in August. While all four serotypes circulated, the predominant serotypes identified were DEN−1 and DEN−2.

The Lao People’s Democratic Republic

Suspected or probable dengue cases are reported through the National Surveillance System for Selected Notifiable Diseases and the Early Warning and Response Network. In 2010, the Lao People’s Democratic Republic reported 22,929 cases (46 fatal), with a peak (n = 1323 cases) during week 33 in August. While all four serotypes circulated, the predominant serotype identified was DEN−1, followed by DEN−2 and DEN−3.

Malaysia

Suspected or probable dengue cases are reported through the National Notifiable Infectious Diseases
Table 1. Cases of dengue, including imported cases, and dengue-attributed deaths in the Western Pacific Region for 2010 (as of 22 May 2011)

<table>
<thead>
<tr>
<th>Countries and areas</th>
<th>No. of cases</th>
<th>Incidence per 100 000</th>
<th>No. of deaths</th>
<th>Case fatality ratio (%)</th>
<th>Population (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia subregion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brunei Darussalam</td>
<td>298</td>
<td>73.17</td>
<td>2</td>
<td>0.67</td>
<td>407</td>
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<td>Cambodia</td>
<td>12 500</td>
<td>83.10</td>
<td>38</td>
<td>0.30</td>
<td>15 042</td>
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<td>China</td>
<td>202</td>
<td>0.01</td>
<td>0</td>
<td>0</td>
<td>1 353 826</td>
</tr>
<tr>
<td>Hong Kong (China)</td>
<td>83</td>
<td>1.18</td>
<td>0</td>
<td>0</td>
<td>7 057</td>
</tr>
<tr>
<td>Japan</td>
<td>243</td>
<td>0.19</td>
<td>0</td>
<td>0</td>
<td>127 029</td>
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<tr>
<td>Republic of Korea*</td>
<td>23</td>
<td>0.05</td>
<td>0</td>
<td>0</td>
<td>48 526</td>
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<tr>
<td>Lao People’s Democratic Republic</td>
<td>22 929</td>
<td>356.36</td>
<td>46</td>
<td>0.20</td>
<td>6 434</td>
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<tr>
<td>Macao (China)</td>
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<td>1.09</td>
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<td>0</td>
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<td>Malaysia</td>
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<td>165.28</td>
<td>134</td>
<td>0.29</td>
<td>27 935</td>
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<tr>
<td>Mongolia</td>
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<td>0</td>
<td>2 703</td>
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<td>Philippines</td>
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<td>144.55</td>
<td>793</td>
<td>0.59</td>
<td>93 639</td>
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<td>Singapore</td>
<td>5 364</td>
<td>110.48</td>
<td>4</td>
<td>0.07</td>
<td>4 855</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>128 831</td>
<td>144.69</td>
<td>55</td>
<td>0.04</td>
<td>89 038</td>
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<td><strong>Total for subregion</strong></td>
<td>352 005</td>
<td>19.81</td>
<td>1 072</td>
<td>0.31</td>
<td>1 777 041</td>
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<td>Pacific subregion</td>
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<td>American Samoa*</td>
<td>51</td>
<td>77.03</td>
<td>0</td>
<td>0</td>
<td>66</td>
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<tr>
<td>Australia</td>
<td>1 171</td>
<td>5.44</td>
<td>0</td>
<td>0</td>
<td>21 527</td>
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<td>Cook Islands</td>
<td>0</td>
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<td>0</td>
<td>0</td>
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<td>0</td>
<td>0</td>
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<td>French Polynesia</td>
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<td>Federated States of Micronesia</td>
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<td>20.71</td>
<td>1</td>
<td>4.35</td>
<td>111</td>
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<td>44.51</td>
<td>0</td>
<td>0</td>
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<tr>
<td>New Zealand</td>
<td>51</td>
<td>1.18</td>
<td>0</td>
<td>0</td>
<td>4 305</td>
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<td>Niue*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commonwealth of the Northern Mariana Islands</td>
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<td>0</td>
<td>0</td>
<td>64</td>
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<tr>
<td>Palau</td>
<td>9</td>
<td>43.94</td>
<td>0</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>Papua New Guinea*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pitcairn Islands*</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Samoa*</td>
<td></td>
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<td></td>
</tr>
<tr>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>536</td>
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<tr>
<td>Tokelau*</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Tonga*</td>
<td>30</td>
<td>28.70</td>
<td>0</td>
<td>0</td>
<td>105</td>
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<tr>
<td>Tuvalu</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>Vanuatu*</td>
<td>192</td>
<td>78.11</td>
<td>0</td>
<td>0</td>
<td>246</td>
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<tr>
<td>Wallis and Futuna*</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Total for subregion</strong></td>
<td>1 902</td>
<td>5.31</td>
<td>1</td>
<td>0.05</td>
<td>35 822</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>353 907</td>
<td>19.52</td>
<td>1 073</td>
<td>0.30</td>
<td>1 812 863</td>
</tr>
</tbody>
</table>

* These data are preliminary and subject to change.

Table 2. Reported number of dengue cases, deaths and case fatality ratios from Cambodia, the Lao People’s Democratic Republic, Malaysia, the Philippines, Singapore, Viet Nam and Australia, 2006–2010

<table>
<thead>
<tr>
<th>Country</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>No. of deaths</td>
<td>CFR* (%)</td>
<td>No. of cases</td>
<td>No. of deaths</td>
<td>CFR* (%)</td>
</tr>
<tr>
<td>Cambodia</td>
<td>16 669</td>
<td>158</td>
<td>0.95</td>
<td>39 851</td>
<td>407</td>
</tr>
<tr>
<td>Lao People’s Democratic Republic</td>
<td>6 356</td>
<td>6</td>
<td>0.09</td>
<td>4 943</td>
<td>4</td>
</tr>
<tr>
<td>Malaysia</td>
<td>38 556</td>
<td>89</td>
<td>0.23</td>
<td>48 846</td>
<td>98</td>
</tr>
<tr>
<td>Philippines</td>
<td>37 101</td>
<td>378</td>
<td>1.02</td>
<td>55 639</td>
<td>533</td>
</tr>
<tr>
<td>Singapore</td>
<td>3 127</td>
<td>10</td>
<td>0.32</td>
<td>8 826</td>
<td>24</td>
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<tr>
<td>Viet Nam</td>
<td>68 532</td>
<td>53</td>
<td>0.08</td>
<td>104 393</td>
<td>88</td>
</tr>
<tr>
<td>Australia</td>
<td>189</td>
<td>0</td>
<td>0.00</td>
<td>316</td>
<td>0</td>
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<tr>
<td><strong>Total</strong></td>
<td>170 530</td>
<td>694</td>
<td>0.41</td>
<td>262 814</td>
<td>1 154</td>
</tr>
</tbody>
</table>

* CFR - case fatality ratio
In 2010, Malaysia reported 46,171 cases (134 fatal). While the number of cases fluctuated throughout the year, the peak ($n = 1159$ cases) was reported during week 34 in August. While all four serotypes circulated, the predominant serotype identified was DEN–1, followed by DEN–3 and DEN–2.

The Philippines

Suspected or probable dengue cases are reported through the Philippines Integrated Disease Surveillance and Response System. In 2010, the Philippines reported 135,355 cases (793 fatal), with a peak ($n = 30,009$) during the month of August. While all four serotypes circulated, the predominant serotype identified was DEN–3.

Singapore

Dengue cases are laboratory-confirmed and reported through the Infectious Diseases Management and Outbreak System. During 2010, Singapore reported 5364 cases (4 fatal), with a peak ($n = 182$) during week 38 in September.

Viet Nam

Suspected or probable dengue cases are reported through the National Notifiable Disease Surveillance system. In 2010, Viet Nam reported 128,831 cases (55 fatal). While all four serotypes circulated, the predominant serotypes identified were DEN–1 and DEN–2.

Pacific subregion

Australia

Dengue cases are laboratory-confirmed and reported through the National Notifiable Diseases Surveillance System. In 2010, Australia reported 1171 cases (none fatal), with a peak ($n = 139$) during the month of November. Dengue activity in Australia is restricted to North Queensland where the vector *Aedes aegypti* is present (the dengue virus itself is not endemic). The predominant serotypes identified from outbreaks in North Queensland were DEN–1 and DEN–2, although all four serotypes have been isolated from imported viraemic cases.

DISCUSSION

In 2010, dengue continued to show an increasing trend in the Western Pacific Region as has been observed in the past decade. The countries with the greatest dengue burden in the Asia subregion, namely the dengue endemic countries of Cambodia, the Lao People’s Democratic Republic, Malaysia, the Philippines, Singapore and Viet Nam, showed an increase in reported number of cases, ranging from 1.1-fold (Malaysia) to 3.2-fold (the Lao People’s Democratic Republic) the number of cases reported in 2009 (Table 1). Importantly, the Lao People’s Democratic Republic also reported an increase in CFR relative to 2009 (Table 1). For Cambodia, the Lao People’s Democratic Republic, the Philippines and Singapore dengue activity followed historic seasonal trends, with peaks occurring shortly after onset of the rainy season during and around the month of August. The expansion of the *Aedes aegypti* habitat is believed to increase overall prevalence of disease in the environment and raise the risk of its spread. From the Pacific subregion, French Polynesia, New Caledonia, Vanuatu and Australia contributed 91% of reported cases, with Australia (North Queensland) reporting more than 1000 laboratory-confirmed cases for two consecutive years.

Sharing of regional surveillance data plays an important role in dengue control. While vector control activities at the local level are essential to interrupt dengue transmission, routine and timely information-sharing of regional data improves countries and areas' understanding of the overall dengue situation, including dengue epidemiology in neighbouring countries or other countries of interest with close trade/travel links. Indeed, dengue does not acknowledge national borders, and in the Pacific islands, dengue activity has been associated with introductions from various locations in Asia.

Comprehensive regional information provides better-informed risk assessments by each country that directly lead to response activities, such as preparation for enhanced education and awareness activities. Regional surveillance data showing continued high level dengue activity have also contributed to the recent launch of the Association of Southeast Asian Nations Dengue Day on 15 June 2011, which aimed at improving advocacy and community participation. Sharing additional surveillance data, such as serotypes and affected age group data, can further improve risk assessments since monitoring these data may reveal important changes or features in dengue epidemiology.

As with any surveillance data, these data have important limitations attributable to changes in reporting behaviour, surveillance systems, misclassifications and
underreporting. For example, a proportion of the excess cases in the Philippines in 2010 (135,355 in 2010 versus 57,819 in 2009) is a result of an ongoing change in the surveillance system. Since 2008, the surveillance system has been transitioning from a sentinel (National Epidemic Sentinel Surveillance System) to an all-case reporting system (PIDSR). The extent of this transition has been variable, with some areas starting the transition earlier than others (personal communication, the Philippines Department of Health).

In addition, as dengue surveillance in Cambodia, the Lao People’s Democratic Republic, Malaysia, the Philippines and Viet Nam is based on suspected or probable cases that are not all laboratory-confirmed, the number of reported cases should be interpreted with caution. Moreover, systematic and representative sampling for laboratory confirmation in some of these countries has been challenging, limiting interpretability of reported serotype data. As dengue surveillance is not standardized across endemic countries, comparisons between countries should also be interpreted with caution. For example, CFRs are affected not only by clinical management but also by case-reporting systems and reporting behaviours of clinicians.

While direct comparisons between countries cannot be made, these data are important for assessing trends both within and across years. The data from 2010 indicate that for the majority of endemic countries dengue activity followed historic seasonality. In addition, increase in the annual trend of reported cases in Singapore and Malaysia appeared to indicate a true increase in 2010 for these countries. As cases are reported from consistent surveillance systems and case definitions, misclassification of cases likely remained constant. To make dengue surveillance useful for timely and effective public health response, trend assessments will continue to be essential both at national and regional levels.

The ongoing dengue burden in the Western Pacific Region underscores the continuing need for region-wide sharing of information on a timely and routine basis. Countries and areas should continue to maintain their surveillance activities and, where they are lacking or deficient, enhance or implement dengue surveillance systems. Enhanced dengue surveillance could also act as a model system for countries where surveillance capacities are limited for endemic infectious diseases; such activities are in line with the biregional Asia Pacific Strategy for Emerging Diseases framework to strengthen national capacities for surveillance and response. Even in countries where dengue is not endemic (e.g. Australia and Japan), the ever-increasing importation of cases highlights the importance of monitoring and reporting of dengue for all countries and areas in the Region. Lastly, to improve preparedness and response activities in the face of the ever-evolving epidemiology of dengue, there is a need for more systematic surveillance and reporting of serotype and age- and sex-stratified data.

Conflicts of Interest
None declared.

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References:
Challenges and future perspective for dengue vector control in the Western Pacific Region

Moh Seng Chang, Eva Maria Christophel, Deyer Gopinath, and Rashid Md. Abdur on behalf of Malaria, Other Vectorborne and Parasitic Diseases, World Health Organization Regional Office for the Western Pacific

Dengue remains a significant public health issue in the Western Pacific Region. In the absence of a vaccine, vector control is the mainstay for dengue prevention and control. In this paper we describe vector surveillance and vector control in the Western Pacific countries and areas.

Vector surveillance and control strategies used by countries and areas of the Western Pacific Region vary. Vector control strategies include chemical, biological and environmental management that mainly target larval breeding sites. The use of insecticides targeting larvae and adult mosquitoes remains the mainstay of vector control programmes.

Existing vector control tools have several limitations in terms of cost, delivery and long-term sustainability. However, there are several new innovative tools in the pipeline. These include Release of Insects Carrying a Dominant Lethal system and Wolbachia, an endosymbiotic bacterium, to inhibit dengue virus in the vector. In addition, the use of biological control such as larvivorous fish in combination with community participation has potential to be scaled up.

Any vector control strategy should be selected based on evidence and appropriateness for the entomological and epidemiological setting and carried out in both inter-epidemic and epidemic periods. Community participation and interagency collaboration are required for effective and sustainable dengue prevention and control. Countries and areas are now moving towards integrated vector management.

BACKGROUND

Dengue fever (DF) and dengue haemorrhagic fever (DHF) are on the increase in Asia and the Pacific. Countries and areas in the World Health Organization (WHO) Western Pacific Region are reporting more cases and an increase in the frequency of epidemics. Four countries in particular, Cambodia, Malaysia, the Philippines and Viet Nam (mainly southern Viet Nam), are facing annual epidemics that constitute over 90% of the total dengue cases reported in the Region.1

Given the lack of a dengue vaccine, control of dengue depends on vector control. Vector control is best achieved through management of breeding sites. The primary goal of vector control activities is to reduce vector population density to levels that are believed to correlate with a lower dengue transmission risk.2 The most important dengue vector in the Western Pacific Region is Aedes aegypti (Stegomyia aegypti), which is predominately found in densely populated urban areas. Dengue outbreaks have also been associated with Aedes albopictus, particularly in China,3 and several other Aedes species found in South Pacific countries and areas may also be competent dengue vectors.4 Aedes breeding tends to occur in household containers.

In this paper we describe dengue vector surveillance and control practices in the Western Pacific Region and provide a perspective for future dengue control.

DENGUE VECTOR SURVEILLANCE

While insufficient to accurately predict the risk of human infection, dengue vector surveillance employs several entomological indicators that have been developed to assess the risk of outbreaks occurring. These include house index, Breteau index, container index and ovitrap indexes that are solely based on entomological parameters and lack epidemiological input. Models have attempted to redress this shortfall, including use of a pupal index that has been shown to be correlated to dengue seroprevalence in a population.5,6 A model employing all three parameters of dengue transmission – vector density, human cases and vector infection rate – would probably be the most accurate...
Chang et al. Dengue control in the Western Pacific Region

in determining outbreak thresholds for early outbreak prediction. Vector surveillance is conducted using these and other indicators in several Western Pacific Region countries and areas (Table 1).

DENGUE VECTOR CONTROL STRATEGIES

Vector control methods and strategies differ across countries and areas in the Western Pacific Region (Table 2). Strategies depend upon specific dengue vector ecology, case burden, availability of resources, feasibility of proper application and the cultural context of the country. An understanding of local mosquito ecology is important for determining an effective, targeted strategy. The trend for dengue vector control in the Region has shifted from relying solely on insecticides to include source reduction, biological control and environmental management through community participation. However, insecticide use is still the mainstay of dengue vector control during outbreaks.

![Table 1. Description of dengue vector surveillance in selected countries and areas of the Western Pacific Region](image-url)

<table>
<thead>
<tr>
<th>Selected country/area</th>
<th>Vector surveillance description</th>
<th>Types of Aedes indices used</th>
<th>Geographical areas</th>
<th>Frequency</th>
</tr>
</thead>
</table>
| **Australia (North Queensland)** | - BG-Sentinel™ or BG traps and net traps for adult vector monitoring  
- Ovitraps (lethal traps) in sentinel urban areas  
- Larval surveys for presence of vectors and to assess residual applications to receptacles  
- Larval surveys, standard ovitraps, BG and Encephalitis Vector Survey traps for vector importation presence | House and Breteau Adult BG trap presence only (vector free but frequent importations) | Selected sites in sentinel urban areas and port areas  
Principal overseas port areas, selected urban sentinel sites | Regular/monthly during summer rainy season and outbreaks  
Weekly to fortnightly |
| **Cambodia** | Larval/pupal surveys in sentinel surveillance sites to assess high-risk areas and mass larvicide control measures | House, Breteau, container and pupal density | Sentinel sites in urban, semi-urban and rural areas | Not regular/Rainy and dry seasons |
| **China** | - Human landing catch  
- Light trap and net trap for vector monitoring | House, Breteau, container and pupal density | Selected sites in urban and semi-urban areas | Not regular/As study projects |
| **Hong Kong (China)** | Routine ovitrap surveillance in sentinel sites to monitor vector density and generate ovitrap index as dengue risk indicator | Ovitrap | Sentinel sites in urban residential areas | Regular, throughout the year |
| **Lao People’s Democratic Republic** | Sentinel surveillance sites to assess high-risk areas and community participation | House, Breteau and container | Sentinel sites in urban, semi-urban and rural areas | Not regular |
| **Malaysia** | Larval surveys to assess the density of vector breeding sites and high risk areas  
- Ovitrap surveys as research projects  
- Surveys as part of epidemic response activities for law enforcement | House, Breteau and container | Urban, suburban and nationwide | Routine |
| **Philippines** | - Larval/pupal surveys in selected sites for community-based vector control  
- Vector surveys as part of entomological research activities  
- Larval surveys to assess the presence of vector, vector activity and distribution, and to monitor breeding habitats | House, Breteau, container and pupal density | Urban, suburban | Not regular |
| **Singapore** | - Ovitrap to assess the effectiveness of control measures and to monitor high-risk areas | House, Breteau, container and ovitrap | Urban, suburban and nationwide | Routine |
| **Viet Nam** | Sentinel surveillance sites to assess high-risk areas and community-based vector control | House, Breteau, container and pupal density | Sentinel sites in urban, semi-urban and rural areas | Not regular |
A systematic literature review and case studies describing dengue vector control services by the WHO Special Programme for Research and Training in Tropical Diseases have been published elsewhere. The following review provides information on national dengue control operational strategies implemented at the programmatic level.

(1) Chemical treatment of breeding sites

Larvicides to prevent vector breeding are used in several countries and areas in the Western Pacific Region. In Cambodia, timely larviciding before the dengue season in targeted, densely populated areas has been designed as a short-term intervention since 2000. The intervention was reported to have reduced the number of dengue cases and deaths by 53%. Targeted containers in stratified dengue high risk areas are treated twice annually to prevent outbreaks. Large containers can also be specifically targeted, both as a preventive method and during outbreaks.

Application to every possible breeding container in the Greater Mekong Subregion countries is not feasible due to cost and operational delivery shortfalls. Larvicides should be used in tandem with community mobilization and environmental management. Larvicides furthermore carry the risk of development of insecticide resistance and community dependence on expensive, centrally planned interventions. Wide-scale outbreaks in Cambodia in 2007, outside the stratified high-risk areas, and presence of abundant discarded containers and cryptic breeding sites underline the possibility of dengue spreading into new rural areas where the control programme cannot easily use larvicides for outbreak mitigation and prevention.

During outbreaks, chemical larvicides are used to target containers breeding vectors in houses near case clusters. While larviciding is effective at lowering vector density, infectious adult mosquitoes are not affected and transmission may continue for the remaining

Table 2. Control of dengue virus vectors \( (Aedes aegypti \text{ and } Aedes albopictus) \) in Western Pacific Region

<table>
<thead>
<tr>
<th>Country/areas</th>
<th>Space spraying (outbreak)</th>
<th>Larviciding (chemical &amp; biological larvicide)</th>
<th>Biological control</th>
<th>Environmental management (source reduction)</th>
<th>Health education and community mobilization</th>
<th>Legislation</th>
<th>Intersectoral and agency collaboration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia (North Queensland)</td>
<td>++</td>
<td>++</td>
<td>+ (guppy fish as operational research)</td>
<td>+</td>
<td>+ (school based)</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Australia (Northern Territory)</td>
<td>++</td>
<td>++</td>
<td>+ (guppy fish as operational research)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cambodia</td>
<td>+</td>
<td>++</td>
<td>+ (school based)</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>China</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Hong Kong (China) &amp; Macau (China)</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lao People’s Democratic Republic</td>
<td>+</td>
<td>+</td>
<td>+ (guppy fish as operational research)</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Fiji</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
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<td>-</td>
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<tr>
<td>Malaysia</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Philippines</td>
<td>+</td>
<td>+</td>
<td>+ (guppy fish as operational research)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Solomon Islands</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Singapore</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Vanuatu</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>+</td>
<td>+</td>
<td>+ (Mesocyclops)</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

** ** Exists and is a regular/core programme activity
* * Exists but irregular, only used under field research condition
- Does not exist

Source: Country Reports, 2008, World Health Organization Western Pacific Region.
lifetime of the infectious adult mosquito. In Australia (North Queensland) a residual insect growth regulator (methoprene) is regularly used in discarded and disused containers, roof gutters, rainwater tanks and other rainwater-collecting containers to reduce overall populations seasonally and for outbreak control.\textsuperscript{9}

The World Health Organization Pesticide Evaluation Scheme recommends several larvicides including temephos, insect growth regulators and \textit{Bacillus thuringiensis} that are safe for drinking-water treatment.\textsuperscript{10} There are reports from Malaysia on the high efficacy of \textit{Bacillus thuringiensis} var. \textit{israelensis}, distributed by space spraying for vector control.\textsuperscript{11,12}

\textbf{(2) Insecticide spraying}

Chemical insecticide spraying is designed to reduce disease transmission by lowering the adult vector population and targeting infectious adults through reducing their longevity. The writers are of the opinion that spraying is recommended only as a method of controlling ongoing or preventing incipient outbreaks through a single, massive reduction in adult vector density. However the practice of indiscriminate or wide-scale outdoor spraying is of questionable effectiveness since many mosquitoes may be inaccessible and would be unaffected. In addition, the insecticidal effects of spraying are transient and depend on persistence of the insecticide used and method of application.

A long timelag between reporting of human cases and commencement of spraying also minimizes the effects of intervention. This lag is likely longest in resource-constrained countries with rural populations where reporting of cases and commencement of vector control activities take longest. Clinicians at lower levels of the health systems may not recognize dengue symptoms, and the surveillance system in rural areas may be relatively poor. In these situations, spraying operations will take longer to implement. Poor functionality of sprayers, insufficient coverage of spraying and incorrect dosage of chemical insecticides coupled with poor public acceptance and compliance also affect the effectiveness of operations. While local teams should have the expertise to conduct spraying effectively, central-level Ministry of Health staff may be required to supervise to ensure the quality of operations.

\textbf{(3) Biological control}

Biological control of dengue vectors is based on the concept of introducing organisms that prey upon, compete with, or otherwise reduce the density of vectors. In the case of \textit{Aedes aegypti}, the immature stages of the vectors in household water containers provide a suitable target for the introduction of biological control agents. Their introduction must be safe, inexpensive, easy to produce on a large scale and be culturally and socially acceptable to the target population. In the case of \textit{Aedes} mosquitoes, certain species of fish and predatory copepods have proven effective.\textsuperscript{13-15}

Viet Nam has experimented with the use of the copepod \textit{Mesocyclops} as a community-based biological control agent.\textsuperscript{13,14} The project yielded promising results, and within three years less than 1.5% of houses were positive for dengue vectors in the project areas. This successful model was due to a combination of vertical and horizontal approaches, identification of key \textit{Aedes} breeding sites and strong multisectoral cooperation. When used in combination with community source reduction, the use of \textit{Mesocyclops} is an easy and inexpensive method of \textit{Aedes aegypti} control that should be effective for many communities in Viet Nam and elsewhere.\textsuperscript{13}

In Cambodia, a successful trial of the effectiveness of introducing larvivorous guppy fish (\textit{Poecilia reticulata}) into water storage containers has taken place in a single commune. The trial was successful, with households receiving the intervention exhibiting a 79.0% reduction in \textit{Aedes} container index compared with control houses.\textsuperscript{15} This trial used community volunteers to colonize and distribute guppies and showed a clear impact on entomological indices in the 14-village trial area. Communities were enthusiastic regarding the intervention which offers greater convenience than emptying/washing containers, and only two to three guppy fish are required to control mosquito and plankton/algal growth in each 200–400 litre water container. To assess the effectiveness of the intervention on a larger scale, a communication for behavioural impact\textsuperscript{16} (COMBI) project advocating the use of guppies in tandem with source reduction is currently being implemented in districts of Cambodia and the Lao People’s Democratic Republic.\textsuperscript{17}

\textbf{(4) Environmental management and vector control}

In some areas of the Greater Mekong Subregion, over 80% of households harbour breeding dengue vectors, largely as a result of water storage practices.\textsuperscript{17} Households often feature water storage containers kept outside. These containers, used to store rain, river or well
water for household use and drinking-water for animals are extremely difficult to protect from Aedes aegypti infestation. In addition, discarded containers, tyres and other vessels collect rainwater during the rainy season, providing excellent Aedes aegypti breeding sites. In some countries and areas, water storage containers are scarce and breeding sites are more difficult to locate. In Macau (China), for example, key breeding sites of Aedes albopictus larvae and pupae include water collection wells of closed underground drains, lotus flower jars, garden stone pools and fountains. In Malaysia, breeding sites are often discarded and neglected containers rather than domestic water storage containers. Other potential breeding sites are containers found in parks, empty land, industry buildings, construction sites, and blocked cement drains and septic tanks. Vector control should be targeted to key breeding sites as identified from vector surveillance.

Environmental management aims to alter the environment to minimize vector breeding sites, especially in close proximity with humans, and therefore minimize human-vector contact. These modifications may be long-lasting measures and include modifying building designs such as roof gutters to prevent Aedes breeding, installing flip type water tank covers to deny gravid female Aedes entry and repairing blocked cement drains. Short-term environmental modification measures involve local agencies and engagement of the community. General household sanitation is key to preventing Aedes breeding in domestic environments, and the local authority’s role is to ensure no accumulation of water containers in public places.

(5) Community mobilization

Community-based dengue vector control using COMBI as a planning tool is being incorporated into dengue control programmes in Malaysia, the Lao People’s Democratic Republic and the Philippines. Since 2007, the Lao People’s Democratic Republic Women’s Union has been involved in community mobilization for dengue awareness and larvae detection in households in provinces. It is also involved in distribution of larvicide for dengue outbreak intervention. Community mobilization and school-based dengue control activities have been also piloted. While COMBI projects, adapted from the field of marketing, have the potential to make a sustained impact on dengue vector density, there has been little evidence of the impact of COMBI interventions on dengue transmission or outbreak prevention. Projects implemented in the Region have lacked sufficient evaluation of the sustainability of behavioural changes or the impact on vector control and dengue transmission. Despite advocacy of community participation and mobilization, communities may be reluctant to take appropriate dengue preventive measures except during outbreaks when the effects of dengue are clearest. In the Greater Mekong Subregion, reports of weekly washing of large water storage containers may not reflect actual community practice. Frequent washing of these large containers is not practical, particularly when they are full of scarce water and are in frequent daily use. COMBI processes should be used to effectively communicate and deliver proven tools for dengue prevention. One of the objectives of the current guppy fish project in Cambodia and the Lao People’s Democratic Republic is to identify a community-based dengue vector control tool and use the COMBI process to deliver this tool in the community and thus achieve behavioural change. In this case, a key behavioural change message has been “inspect your water containers for guppy fish on a weekly basis.”

INTERAGENCY COLLABORATION FOR DENGUE CONTROL IN THE REGION

The WHO Asia-Pacific Dengue Strategic Plan (2008–2015) consists of six components; two of these related to vector control are integrated vector management (IVM) and social mobilization and communication. These dengue control activities require interagency collaboration and partnership with other agencies in promoting community-based dengue control. Many countries and areas of the Western Pacific Region use this approach.

Dengue control activities in cities and townships in Malaysia are the responsibility of local authorities. The Minister of Local Government and Housing has equal responsibility with the Ministry of Health for dengue
control. Other agencies involved in dengue prevention and control are the Ministry of Education, Ministry of Environment, Judicial Department and community organization groups. The Ministry of Agriculture is the pesticide regulatory agency. However, there is also a pesticide board responsible for pesticide registration and monitoring use. Most recently, the Ministry of Health is adapting COMBI planning tools aimed at behavioural change in several states in Peninsular Malaysia.

In Australia, Queensland Health has formulated a Dengue Fever Management Plan for North Queensland where *Ae. aegypti* is widespread. The plan focuses on disease surveillance, mosquito control and surveillance and education. Mosquito control is managed by a special unit of Queensland Health, the Dengue Action Response Team (DART). DART operates under the Queensland Public Health Act 2005 that allows the right of access to all yards (excluding houses) to set lethal ovitraps and apply pesticides to any container with mosquitoes.9

In 2002, the Fifty-fifth World Health Assembly adopted resolution WHA55.17 which addressed dengue and dengue haemorrhagic fever prevention and control,22 thereby creating a political environment supportive of international, regional and national dengue activities. In response to this resolution, the Government of Cambodia worked in collaboration with international and bilateral agencies to strengthen the surveillance capacity of the National Dengue Control Programme, to intensify training on clinical management of dengue haemorrhagic fever and to develop, finance and begin implementation of a five-year vector control plan from 2001. A national dengue control committee was set up and established at Ministry level to plan, coordinate and implement the national strategy. Based on vector ecology, dengue endemicity and the socioeconomic situation in Cambodia, the programme focused on lowering epidemic potential through timely application of larvicide via mobilization of thousands of citizens, including local authorities, community volunteer networks and Red Cross workers. In collaboration with the Ministry of Education, School Health Department, a school-based dengue control pilot project was launched in 2005. Several community-based vector control projects have also been implemented and are undergoing field trials, including community use of insecticidal impregnated jar covers, integrated vector control using guppy fish and source reduction activities.23

**FUTURE PERSPECTIVE**

Despite recent heightened awareness for dengue prevention, various challenges still exist. These include inadequate funding and resources and the lack of a sound strategy to respond to the increasing problem of dengue outbreaks in a growing number of geographical areas. Rapid urbanization, lack of basic sanitation, increased mobility of populations and international travel has compounded the problem in some countries and areas, and there is no promising solution for sustainable control of dengue vectors. Given the complexity of dengue vector control at national level, a well-organized dengue control programme should be established to collaborate with different sectors, ministries, agencies and partners to plan, implement and facilitate these activities.

For vector control, there is a need for increased capacity in outbreak response as a component of a three-pronged strategy. This strategy should include community-based larvae control (using environmental management and other technologies as appropriate), adult mosquito management (including research into novel insecticides and their application) and use of personal protection (including research on repellents, adult reduction devices and their mode of delivery).

Preventive activities should be built into existing health care systems and be well coordinated within primary health care activities rather than within the dengue control programme of Ministries of Health. WHO is advocating Integrated Vector Management (IVM) as a further method of dengue vector control.24 IVM is defined as “a rational decision-making process for the optimal use of resources for vector control.” The important attributes of IVM are advocacy, social mobilization and legislation, collaboration within the
health sector and with other sectors, an integrated intervention methods approach, evidence-based decision-making and capacity-building. IVM is suited to dengue management and control programmes in dengue endemic countries and should be used when planning dengue prevention in the Region. To improve the efficiency and effectiveness of dengue vector control, increasing the capacity of countries to implement IVM is critical. The basic elements of dengue control under IVM are to adopt evidence-based selection and delivery of different interventions (or combinations of interventions) based on local settings to increase country vector control delivery capacity in all geographical areas and to implement monitoring and evaluation tools.

New vector control tools for *Aedes aegypti* population suppression and replacement are currently under investigation. The use of Sterile Insect Technique is not a new approach, and it has been used for insect population control against a wide range of agriculture pest insect species. The recently developed Release of Insects Carrying a Dominant Lethal (RIDL) system incorporates a novel genetic sexing system for mass rearing of male mosquitoes. Under this new technology, a lethal gene was micro-injected into the eggs of *Aedes aegypti*. The gene subsequently integrated into the genome of the mosquito. The gene regulates the production of toxic metabolites in the larval stage, killing the larva. The antibiotic tetracycline is used to rear larvae and to maintain the mosquito in the laboratory. This antibiotic inhibits the lethal gene and produces no toxin, allowing larvae to develop fully into adults. In actual control, RIDL males will be released to mate with wild females. Fertilized females will produce eggs that hatch into larvae carrying the RIDL gene. All those carrying the gene will die at late larval or early pupal stage. The Malaysia Institute for Medical Research (IMR) has conducted this project in three phases: (1) establishment of the transgenic Malaysian strain of *Aedes aegypti*; (2) simulation release trial inside a field house; and (3) field release in a suitable experimental field site. Currently IMR is implementing the third phase.

Another development in terms of novel vector control is the discovery that the naturally occurring endosymbiotic bacterium *Wolbachia* – commonly present in insect populations – can inhibit replication of the dengue virus in *Aedes aegypti* mosquitoes. The idea is to introduce these strains of *Wolbachia* into wild populations of *Aedes aegypti*, potentially replacing field populations in a way that could suppress or even possibly eliminate dengue transmission.

Vector surveillance must also be improved, including data on key and target container types for better breeding site management. A geographic information system (GIS)-based approach to dengue control and surveillance can link relevant spatial data to identify key patterns and relationships, aiding in planning and strategic decision-making. Thematic maps can be produced to visualize the spatial distribution of dengue vectors in relation to relevant environmental and climatic indicators. Similarly, dengue cases and vector densities can be mapped to view the spatial patterns of dengue distribution over time and to monitor potential movements of dengue transmission foci after outbreaks have been identified. Through the combination and integration of detailed spatial information into a centralized GIS database, programme managers will be equipped with a simple yet powerful decision-making, planning, surveillance and community education tool for dengue management.

**CONCLUSIONS**

Although intense efforts are under way to develop a vaccine, there is neither vaccine to prevent dengue nor are there any effective antiviral drugs to treat the disease. To minimize the impact of dengue outbreaks, countries and areas should strengthen their vector control programmes, both during inter-epidemic and epidemic periods. Control strategies should use integrated approaches with evidence-based selection and delivery of different interventions or combinations of interventions adapted to different entomological and epidemiological settings. Dengue prevention and control should include individuals, families and the wider community and encourage community participation to have the best chances of success.

**Conflict of interest**

None declared.

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**References:**


Regional Analysis

Male–female differences in the number of reported incident dengue fever cases in six Asian countries

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Introduction. Demographic factors, such as age and sex, are associated with the likelihood of exposure to \textit{Aedes aegypti}, the vector for dengue. However, dengue data disaggregated by both sex and age are not routinely reported or analyzed by national surveillance systems. This study analysed the reported number of incident dengue cases by age and sex for six countries in Asia.

Methods. Data for the Lao People’s Democratic Republic, the Philippines, Singapore and Sri Lanka were obtained from DengueNet; the number of male and female dengue cases was available for four age groups (< 1, 1–4, 5–14 and \(\geq 15\) years) over a cumulative period of six to 10 years. Data for Cambodia (2010) and Malaysia (1997–2008) were obtained from their respective ministries of health.

Results. An excess of males was found among reported dengue cases \(\geq 15\) years of age. This pattern was observed consistently over several years across six culturally and economically diverse countries.

Discussion. These data indicated the importance of reporting data stratified by both sex and age since collapsing the data over all ages would have masked some of the male-female differences. In order to target preventive measures appropriately, assessment of gender by age is important for dengue because biological or gender-related factors can change over the human lifespan and gender-related factors may differ across countries.

Dengue is a tropical and subtropical mosquito-borne infection that can cause severe illness and death. During the last 30 years, dengue fever has dramatically expanded its geographical range and shortened its epidemic cycle in many places. According to the World Health Organization (WHO), dengue is endemic in over 100 countries and approximately two-fifths of the world’s population is currently at risk for dengue fever with an estimated 50 million infections annually.\textsuperscript{1} Among the estimated 2.5 billion people at risk globally for dengue, about 1.8 billion (i.e. more than 70%), reside in Asia Pacific countries.\textsuperscript{2}

The most important vector for dengue, \textit{Aedes aegypti}, is a predominantly urban mosquito species that favours particular environments such as locations where water storage is common and waste disposal services are inadequate.\textsuperscript{1,3} While exposure to such environments may be related to specific demographic factors such as age and sex, there is a scarcity of sex-specific dengue data. Indeed, sex-disaggregated dengue data are not routinely reported or analysed by surveillance systems. The few studies from Asia, such as those from Singapore, that have examined male and female dengue incidence, have tended to find greater male incidence.\textsuperscript{4} Differences in dengue incidence have been attributed to gender-related differences in exposures such as time away from home.\textsuperscript{4,5} As gender roles, and thus exposures, change over the human lifespan, it is important to examine dengue cases by both sex and age. While there are recent studies that provide age-\textsuperscript{6} or sex-specific\textsuperscript{3} incident dengue surveillance data, few studies provide incident dengue data stratified by both age and sex. This study describes the reported number of incident dengue cases by age and sex for six countries in Asia.

METHODS

The current study analysed national surveillance data on the annual number of reported dengue cases by age and sex for six Asian countries. Reported cases included all reported dengue fever cases, dengue haemorrhagic fever
Male–female differences in dengue incidence in Asia

Anker and Arima

cases and cases of dengue shock syndrome. The six countries were selected because their data either were available in DengueNet (part of the WHO Global Atlas that contains national data on select health conditions provided by the ministries of health of participating countries) or were provided to the WHO Western Pacific Regional Office by their ministries of health. Data for the Lao People’s Democratic Republic, the Philippines, Singapore and Sri Lanka were from DengueNet. For these four countries, the number of male and female dengue cases was reported for four age groups (<1, 1–4, 5–14, and ≥15 years) over a period of six to 10 years. Data from Cambodia and Malaysia were provided directly to WHO by their ministries of health. For Cambodia, male and female cases for age groups ≤4, 5–9, 10–14, and ≥15 years were available for 2010 (through 24 December 2010). For Malaysia, the reported number of dengue cases from 1997 to 2008 was available by both sex and age-group separately but not in a form stratified for both. Subnational data were available for four countries. This included the 18 provinces of the Lao People’s Democratic Republic, the 15 states of Malaysia (for 2007 and 2008), the 16 regions of the Philippines and the nine provinces of Sri Lanka. For the Philippines, DengueNet used the same administrative regions that were in existence in 1998, the first year data were submitted to DengueNet from the Philippines.

Since the implications of sex and gender for infectious disease differ with age, age groups were examined separately. Sex refers to biological characteristics of males and females while gender refers to male and female norms that are socially and culturally constructed. For each country and age group, χ² goodness of fit tests were used to compare the observed proportion of males among reported dengue cases to the expected proportion of males in the general population for each age group (Table 1). The proportion of men in the general population for each age group is also provided for comparison. The number and percent male of dengue cases for each subnational administrative region of the Lao People’s Democratic Republic, the Philippines and Sri Lanka, for the ≥15 year age group and for all age groups combined were calculated (Table 2). Results for Malaysia are presented separately (Table 3).

The Lao People’s Democratic Republic

Male–female ratios in dengue cases reported from the Lao People’s Democratic Republic were variable over time and location (Tables 1 and 2). From 2000 to 2006, among infants, percent male of reported cases was similar to the percent male in the general population, and no significant differences were found for any year or for all years combined. There was a small excess of reported male cases among 1–4 year olds, and this male excess was statistically significant for all years combined and for five of the seven years...
Anker and Arima

Male-female differences in dengue incidence in Asia

(Table 1). For 5–14 year olds, there was a slightly lower than expected proportion of males among reported cases. However, results were inconsistent from year to year, with some years reporting proportionately more and others proportionately fewer male cases than expected. The most pronounced difference in the Lao People’s Democratic Republic was found among those ≥15 years of age (58% male cases compared to 49% male in the general population); a significant male excess in this age group was observed in four of the seven years assessed. Much of the male excess in this age group was driven by the larger than expected male cases who were ≥15 years of age in the regions of Savannakhet Province and Vientiane Municipality (Table 2).

The Philippines

The age and sex distribution of reported dengue cases was consistent for 1998–1999 and 2001–2005 in the

Table 1. Reported number of dengue cases, percent male of reported cases, and percent male in the general population, by age group and year for the Lao People’s Democratic Republic, the Philippines, Singapore, Sri Lanka and Cambodia

<table>
<thead>
<tr>
<th>Country/ year</th>
<th>&lt;1</th>
<th>1 to 4</th>
<th>5 to 14</th>
<th>≥15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lao People’s Democratic Republic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>67</td>
<td>47.8</td>
<td>124</td>
<td>56.5</td>
</tr>
<tr>
<td>2001</td>
<td>179</td>
<td>53.6</td>
<td>427</td>
<td>61.4***</td>
</tr>
<tr>
<td>2002</td>
<td>581</td>
<td>48.5</td>
<td>1 213</td>
<td>59.2**</td>
</tr>
<tr>
<td>2003</td>
<td>1 052</td>
<td>52.0</td>
<td>3 876</td>
<td>53.0*</td>
</tr>
<tr>
<td>2004</td>
<td>200</td>
<td>55.0</td>
<td>502</td>
<td>56.0*</td>
</tr>
<tr>
<td>2005</td>
<td>551</td>
<td>48.8</td>
<td>1 051</td>
<td>48.1</td>
</tr>
<tr>
<td>2006</td>
<td>712</td>
<td>53.1</td>
<td>1 133</td>
<td>53.9*</td>
</tr>
<tr>
<td>Total</td>
<td>3 342</td>
<td>51.3</td>
<td>8 326</td>
<td>54.1***</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Populationa</th>
</tr>
</thead>
<tbody>
<tr>
<td>51.1</td>
</tr>
</tbody>
</table>

| Philippines |
| 1998 | 973 | 58.1*** | 6 451 | 50.8 | 19 818 | 49.7*** | 8 406 | 54.3*** |
| 1999 | 242 | 57.4 | 1 785 | 50.8 | 5 021 | 50.9 | 2 358 | 58.9*** |
| 2000 | 607 | 52.1 | 3 814 | 50.7 | 13 399 | 50.4 | 7 132 | 58.4*** |
| 2001 | 361 | 53.5 | 3 055 | 50.5 | 8 645 | 50.6 | 4 428 | 58.2*** |
| 2002 | 650 | 53.4 | 4 866 | 50.9 | 15 749 | 50.5 | 8 260 | 56.2*** |
| 2003 | 561 | 50.4 | 3 583 | 49.7 | 12 426 | 49.9* | 6 470 | 58.4*** |
| 2004 | 806 | 55.3* | 4 915 | 51.0 | 17 202 | 50.5 | 10 472 | 57.8*** |
| Total | 4 200 | 54.5*** | 28 469 | 50.7 | 92 260 | 50.3*** | 47 526 | 57.2*** |

| Populationa |
| 51.3 | 51.5 | 51.0 | 50.0 |

| Singapore |
| 1999 | 6 | 66.7 | 16 | 62.5 | 129 | 61.2* | 1 204 | 68.1*** |
| 2000 | 5 | 40.0 | 17 | 52.9 | 96 | 58.3 | 555 | 66.3*** |
| 2001 | 5 | 80.0 | 27 | 66.7 | 243 | 58.0 | 2 097 | 61.9*** |
| 2002 | 12 | 33.3 | 23 | 65.2 | 429 | 63.2*** | 3 481 | 64.8*** |
| 2003 | 22 | 59.1 | 30 | 56.7 | 532 | 56.0* | 4 204 | 58.7*** |
| 2004 | 22 | 81.8** | 87 | 52.9 | 1 223 | 59.7*** | 8 127 | 61.8*** |
| 2005 | 32 | 50.0 | 160 | 56.9 | 2 126 | 54.1* | 11 891 | 58.3*** |
| Total | 104 | 58.7 | 360 | 57.2* | 4 778 | 57.0*** | 31 559 | 60.7*** |

| Populationa |
| 51.7 | 51.6 | 51.7 | 50.0 |

| Sri Lanka |
| 1996 | 6 | 50.0 | 191 | 45.5 | 506 | 43.3*** | 398 | 58.3*** |
| 1997 | 11 | 36.4 | 142 | 45.8 | 341 | 48.7 | 285 | 69.5*** |
| 1998 | 24 | 54.2 | 218 | 51.4 | 479 | 50.1 | 249 | 66.7*** |
| 1999 | 27 | 59.3 | 219 | 44.7 | 469 | 55.7* | 417 | 63.8*** |
| 2000 | 45 | 51.1 | 320 | 50.0 | 856 | 48.1 | 1 134 | 61.6*** |
| 2001 | 28 | 60.7 | 248 | 46.0 | 687 | 47.6 | 1 590 | 61.8*** |
| 2002 | 38 | 57.9 | 209 | 45.9 | 665 | 44.8** | 2 011 | 59.1*** |
| 2003 | 16 | 37.5 | 106 | 58.5 | 356 | 47.8 | 1 119 | 63.6*** |
| 2004 | 33 | 60.6 | 236 | 47.5 | 878 | 49.5 | 2 623 | 61.8*** |
| 2005 | 28 | 50.0 | 115 | 49.6 | 235 | 50.2 | 654 | 62.7*** |
| Total | 256 | 53.9 | 2 004 | 48.1** | 5 472 | 48.4*** | 10 480 | 61.8*** |

| Populationa |
| 50.9 | 50.9 | 50.9 | 49.4 |

| Cambodia |
| 2010 | 3 948* | 50.1 | 8 123 | 48.9*** | 276 | 60.1*** |

| Populationa |
| 51.0 | 51.0 | 48.0 |

---

* These are the only countries with data by age group. See table 3 for data for total population of Malaysia.

** Population data are for the year 2000.

*** Data from the Philippines are not available in DengueNet for the year 2000.

**** Reported cases for age group 0-4 years. Reported dengue cases for age group <1 were not available for Cambodia.

*, **, and *** denote years and age groups for which the percent male among reported dengue cases was significantly different from the percent male in the population at the α = 0.05, 0.01, and 0.001 levels, respectively.
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Philippines. Reported number of cases by age and sex was not available for the year 2000. Over these seven years, there was a significant excess of male cases among those ≥ 15 years of age and among infants (Table 1). Subnational data on the sex distribution of cases ≥ 15 years of age were also consistent, showing an excess of male cases in all regions in this age group (Table 2). For the 1–4 and 5–14 year age groups, the


<table>
<thead>
<tr>
<th>Country</th>
<th>Administrative region or province</th>
<th>Number of cases, age ≥15 years</th>
<th>% Male cases, age ≥15 years</th>
<th>Number of cases, all ages</th>
<th>% Male cases, all ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lao People’s Democratic Republic</td>
<td>Attapeu</td>
<td>95</td>
<td>42.1</td>
<td>269</td>
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</tr>
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<td>Bokeo</td>
<td>18</td>
<td>44.4</td>
<td>68</td>
<td>57.4</td>
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<tr>
<td></td>
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<td>49.7</td>
<td>2 837</td>
<td>50.9</td>
</tr>
<tr>
<td></td>
<td>Champasack</td>
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<td>6 358</td>
<td>48.0</td>
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<tr>
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<td>69</td>
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<td>52.3</td>
<td>2 705</td>
<td>54.2</td>
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<tr>
<td></td>
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<td>59.4</td>
<td>14 719</td>
<td>56.3</td>
</tr>
<tr>
<td></td>
<td>Vientiane Special Reg</td>
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<td>57</td>
<td>56.1</td>
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<tr>
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<td>Xiengkhuang</td>
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<td>66.7</td>
<td>3</td>
<td>66.7</td>
</tr>
<tr>
<td>All regions combined</td>
<td></td>
<td>22 347</td>
<td>57.9</td>
<td>47 483</td>
<td>54.5</td>
</tr>
<tr>
<td></td>
<td>% Male in population ≥ 15 years</td>
<td>49.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Philippines</td>
<td>Autonomous Region of Muslim Mindanao</td>
<td>333</td>
<td>58.3</td>
<td>1 106</td>
<td>53.4</td>
</tr>
<tr>
<td></td>
<td>Bicol</td>
<td>2 687</td>
<td>52.9</td>
<td>8 713</td>
<td>51.7</td>
</tr>
<tr>
<td></td>
<td>Cordillera Administrative Region</td>
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<td>55.7</td>
<td>3 668</td>
<td>55.0</td>
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<tr>
<td></td>
<td>Cagayan Valley</td>
<td>3 292</td>
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<td>52.1</td>
</tr>
<tr>
<td></td>
<td>Catandba</td>
<td>1 062</td>
<td>59.0</td>
<td>3 717</td>
<td>52.5</td>
</tr>
<tr>
<td></td>
<td>Central Luzon</td>
<td>8 073</td>
<td>59.9</td>
<td>25 274</td>
<td>53.5</td>
</tr>
<tr>
<td></td>
<td>Central Mindanao</td>
<td>2 442</td>
<td>57.7</td>
<td>5 975</td>
<td>53.1</td>
</tr>
<tr>
<td></td>
<td>Central Visayas</td>
<td>3 552</td>
<td>57.4</td>
<td>20 120</td>
<td>50.9</td>
</tr>
<tr>
<td></td>
<td>Eastern Visayas</td>
<td>2 463</td>
<td>55.5</td>
<td>11 399</td>
<td>52.0</td>
</tr>
<tr>
<td></td>
<td>Ilocos</td>
<td>632</td>
<td>56.1</td>
<td>3 847</td>
<td>52.7</td>
</tr>
<tr>
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<td>National Capital Region</td>
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<td>58.6</td>
<td>27 946</td>
<td>53.7</td>
</tr>
<tr>
<td></td>
<td>Northern Mindanao</td>
<td>3 193</td>
<td>55.4</td>
<td>14 811</td>
<td>51.0</td>
</tr>
<tr>
<td></td>
<td>Southern Mindanao</td>
<td>3 174</td>
<td>56.7</td>
<td>12 256</td>
<td>51.0</td>
</tr>
<tr>
<td></td>
<td>Southern Tagalog</td>
<td>1 498</td>
<td>63.5</td>
<td>7 541</td>
<td>52.9</td>
</tr>
<tr>
<td></td>
<td>Western Mindanao</td>
<td>2 593</td>
<td>52.7</td>
<td>7 360</td>
<td>51.3</td>
</tr>
<tr>
<td></td>
<td>Western Visayas</td>
<td>1 545</td>
<td>54.7</td>
<td>8 506</td>
<td>51.7</td>
</tr>
<tr>
<td>All regions combined</td>
<td></td>
<td>47 450</td>
<td>57.1</td>
<td>172 288</td>
<td>52.3</td>
</tr>
<tr>
<td></td>
<td>% Male in population ≥ 15 years</td>
<td>50.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>Central</td>
<td>666</td>
<td>63.5</td>
<td>1 163</td>
<td>56.7</td>
</tr>
<tr>
<td></td>
<td>Eastern</td>
<td>209</td>
<td>61.7</td>
<td>428</td>
<td>62.4</td>
</tr>
<tr>
<td></td>
<td>North Central</td>
<td>236</td>
<td>68.2</td>
<td>346</td>
<td>63.0</td>
</tr>
<tr>
<td></td>
<td>North Western</td>
<td>730</td>
<td>64.0</td>
<td>1 117</td>
<td>63.3</td>
</tr>
<tr>
<td></td>
<td>Northern</td>
<td>149</td>
<td>59.7</td>
<td>187</td>
<td>59.4</td>
</tr>
<tr>
<td></td>
<td>Sabaragamuwa</td>
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<td>63.4</td>
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</tr>
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<td>Southern</td>
<td>953</td>
<td>65.9</td>
<td>1 440</td>
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<td>Uva</td>
<td>132</td>
<td>66.7</td>
<td>213</td>
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</tr>
<tr>
<td></td>
<td>Western</td>
<td>3 349</td>
<td>59.1</td>
<td>7 407</td>
<td>53.9</td>
</tr>
<tr>
<td>All regions combined</td>
<td></td>
<td>6 858</td>
<td>61.8</td>
<td>12 946</td>
<td>55.9</td>
</tr>
<tr>
<td></td>
<td>% Male in population ≥ 15 years</td>
<td>49.4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

\[a\] Reported numbers of dengue cases by sex missing for Xaysomboun Special Region for the year 2006.

\[b\] Total number of cases reported from regions was less than the total number reported at the national level in Table 1.

\[c\] No provincial data available for Sri Lanka for the years 2004 and 2005.
proportions of males among reported cases were similar to the male proportion in the population, differing by less than 1% (Table 1).

**Singapore**

Among the countries assessed, Singapore had the largest proportion of male dengue cases reported. The proportion of men among reported cases was significantly larger relative to the general population, ranging from 57% in the 5–14 year age group to 61% in the ≥15 year age group. The difference was significant in all age groups, except in infants where the numbers were small, with a consistent pattern over time from 1999 to 2005 (Table 1).

**Sri Lanka**

In Sri Lanka, there was a consistent and significantly larger proportion of males among reported dengue cases than expected in the ≥15 year old age group from 1996 to 2005 (Table 1). This male excess was reported in every province (Table 2). Among 1–4 and 5–14 year olds, there were significantly fewer male cases than expected, although there was some annual variation.

Dengue epidemiology in Sri Lanka underwent changes during 1996–2005. The proportion of reported cases from Western Province, which contains the country’s largest city, Colombo, decreased from 84% in 1999 to 37% in 2003 (data not shown). The age distribution of reported cases changed from children less than 15 years of age making up more than 60% of cases in 1996–1999 to less than 40% of cases in 2001–2005 (Table 1).

**Malaysia**

In Malaysia, only the total number of reported male and female dengue cases was available from 1997–2008 (Table 3). The majority of reported cases were persons over 15 years of age (between 76% and 82% for the years 1997–2008; data not shown). Although dengue data stratified for both age and sex were not available for Malaysia, the majority of reported cases were consistently male, significantly more than expected (Table 3). For each of the two years for which subnational data were available, there was a consistent pattern of excess in reported male cases from each state; for 2007, percent male ranged from 56% to 72% with an overall 59% and for 2008, percent male ranged from 58% to 67% with an overall 62%.

**Cambodia**

Dengue data for Cambodia were available for 2010. In Cambodia, 6116 of 12 347 (49.6%) cases reported in 2010 (through 24 December 2010) were male. The proportion of reported male cases by age group were: 50.1% among those aged 4 years or less, 48.9% among those aged 5–14 years (significantly less than expected), and 60.1% among those aged 15 years or more (significantly more than expected) (Table 1).

**DISCUSSION**

This study, based on reported dengue cases from national surveillance systems, found a consistent and significant excess among males ≥15 years of age. This pattern was consistent over a period of six to 10 years in three culturally and economically diverse countries and over geographically diverse subnational areas within two countries. Although age- and sex-stratified data were not available for Malaysia, most of reported cases were for persons over 15 years of age, and there was a consistent excess of male cases over a 12-year period. In a previous study of dengue incidence in Malaysia between 1973 and 1987 the majority of reported cases were also found to be male. The observed overall pattern of male excess among reported cases in older age groups agrees with

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**Table 3. Total number of reported dengue cases and percent male among reported dengue cases, Malaysia, 1997–2008**

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of cases</th>
<th>% male cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>19 429</td>
<td>54.4*</td>
</tr>
<tr>
<td>1998</td>
<td>27 381</td>
<td>55.6*</td>
</tr>
<tr>
<td>1999</td>
<td>10 146</td>
<td>59.6*</td>
</tr>
<tr>
<td>2000</td>
<td>7 103</td>
<td>59.2*</td>
</tr>
<tr>
<td>2001</td>
<td>16 368</td>
<td>56.2*</td>
</tr>
<tr>
<td>2002</td>
<td>32 767</td>
<td>54.7*</td>
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<td>2005</td>
<td>39 686</td>
<td>58.1*</td>
</tr>
<tr>
<td>2006</td>
<td>38 556</td>
<td>58.1*</td>
</tr>
<tr>
<td>2007</td>
<td>48 846</td>
<td>59.3*</td>
</tr>
<tr>
<td>2008</td>
<td>49 335</td>
<td>61.5*</td>
</tr>
</tbody>
</table>

Percent male in Population = 50.8

*Denotes years and age groups for which the percent male among reported cases was significantly different from the percent male in the general population at the α=0.001 level.

Malaysia did not report male and female dengue cases by age group.

Population data are for the year 2000.
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previous studies in Singapore\textsuperscript{4,10,11} and has also been found in more recent dengue surveillance data from the Philippines for 2010 (the Philippines Department of Health, personal communication) and Singapore for 2009.\textsuperscript{12} Taken together, these findings suggest that there may be gender-related differences in dengue incidence, which might be due to exposure differences among older adolescents and adults. These results in Asia are in contrast to studies in South America, which have found either equal proportions of male and female dengue cases or a greater proportion of female cases.\textsuperscript{5,7,13–15}

The reasons for the excess of reported male dengue cases among older adolescents and adults in Asia observed in this study need further exploration. In Singapore, a careful analysis attributed greater reported male incidence of dengue from 1998 to 2000 to greater male exposures to dengue-carrying mosquitoes during daytime hours either at the workplace or while travelling to and from work.\textsuperscript{4} This theory is supported by the fact that aggressive public health measures in Singapore have been able to greatly reduce the mean number of mosquitoes in the home,\textsuperscript{10} and the fact that the labour force in Singapore has more males than females.\textsuperscript{4} However, this hypothesis has been questioned by a recent serological study of adults by Yew et al.,\textsuperscript{11} which found no significant differences between males and females in recent dengue infection, despite the excess of male cases reported during the same year the serological study was conducted. Yew et al. suggested that male–female differences in the use of health services and/or male–female differences in disease severity might account for this discrepancy. For example, working adults in Singapore (who are more likely to be male)\textsuperscript{4,16} may be more likely to seek treatment and be reported to the Ministry of Health when ill because they require medical certification for absences.

Yew et al. did find males to be significantly more likely to have had a past dengue infection in a multivariate analysis which adjusted for ethnicity, age, and work status.\textsuperscript{11} The authors felt that the greater presence of males in the workforce could not explain this difference, however, since housewives, retirees and the unemployed were found to have proportionally larger seropositivity than those employed. Moreover, after adjusting for work status, male gender remained significantly associated with past infection status, which indicates that the higher seroprevalence could not be fully or explained by employment status alone. It was suggested that movement history should be studied as a possible contributing factor of dengue infection in Singapore.

For those $\leq 15$ years of age, sex differences in the reported number of cases were less striking. The differences found among those aged 1–4 years and 5–14 years were not consistent, and the magnitude of the difference was relatively small, except in Singapore. However, the excess number of male infants with dengue in the Philippines and Singapore deserves further study. Although there were relatively few reported cases among infants, the relatively high dengue case fatality during infancy makes infants an important risk group. Male excess in infants was also reported in more recent dengue surveillance data from the Philippines for 2010 (the Philippines Department of Health, personal communication) and for those aged 4 years or less from Singapore for 2009.\textsuperscript{12}

Since the data assessed in this paper are based on national surveillance systems, they are subject to the limitations inherent in surveillance data such as underreporting, misreporting and reporting biases. Evidence from several studies suggests that only a minority of dengue infections are reported to surveillance systems, partly because a large proportion of dengue infections are either subclinical or asymptomatic.\textsuperscript{11} While differential reporting by sex is unlikely to fully explain the observed excess in adult males, any gender bias that exists in the use of health services could affect the number of reported male and female cases. For example, since adults appear to be more susceptible than children to developing symptoms after dengue virus infection,\textsuperscript{5,17,18} and if adult men are more likely to seek health care than adult women, there may be a larger number of reported adult male cases even if there is no difference in the underlying incidence rates. An important limitation was our inability to assess sex differences in reported dengue cases among adults more precisely. This was not ideal, particularly for comparing working adults and retirees. Since the epidemiology of dengue is rapidly changing, and has evolved into more of an adult disease rather than a paediatric disease in some countries,\textsuperscript{6,10} continued monitoring and assessment by appropriate age groups are important. Lastly, there are also likely to be variations over time and across countries in reporting practices and case definitions. While one of the aims of DengueNet was to harmonize case definitions, case definitions are not provided on DengueNet. Due to such
variability, it is inappropriate to combine data from all countries. The fact that we found a consistent excess of males in the older age group across many years, and in both national and subnational data from several Asian countries, is an important strength of this study.

In conclusion, the current study found a consistent pattern of male predominance in the reported number of incident dengue cases among persons 15 years or older in several Asian countries. Since collapsing the data over all ages would have masked some of the observed differences, the findings indicate the importance of reporting sex and age-stratified data for dengue surveillance. Assessment of how dengue differs for males and females by age is important because biological and gender-related factors can change over the human lifespan, and gender-related factors can differ across countries. Further research is required to identify the cause(s) of such sex-specific differences to target preventive measures to reduce the dengue burden in the region.

Conflicts of interest
None declared.

Funding
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References:
Original Research

Epidemiological characteristics of the 2005 and 2007 dengue epidemics in Singapore – similarities and distinctions

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Introduction: We investigated the epidemiological features of the 2007 dengue outbreak to determine the factors that could have triggered it two years after the previous large outbreak in 2005.

Methods: All laboratory-confirmed cases of dengue reported during the year, as well as entomological and virological data, were analysed.

Results: A total of 8826 cases including 24 deaths were reported in 2007, giving an incidence of 192.3 cases per 100,000 residents and a case-fatality rate of 0.27%. The median age of the cases was 37 years (interquartile range 25 to 50), with an age range from two days to 101 years, which was higher than the median age of 31 years (interquartile range 20 to 42), with a range from four days to 98 years, in 2005. The overall Aedes premises index in 2007 was 0.68%, lower than the 1.15% observed in 2005. The predominant dengue serotype in 2007 was dengue virus DENV-2 which re-emerged with a clade replacement in early 2007, and overtook the predominant serotype (DENV-1) of 2005. Seroprevalence studies conducted in the three largest outbreak clusters revealed that 73.2% of residents with recent infection were asymptomatic.

Discussion: With the exception of an increase in the median age of the cases, and a change in the predominant dengue serotype, the epidemiological features of the 2007 epidemic were largely similar to those of 2005. Singapore remains vulnerable to major outbreaks of dengue, despite sustained vector control measures to maintain a consistently low Aedes premises index.

The four serotypes of dengue virus (DENV) (family Flaviviridae) are transmitted from infected to susceptible humans primarily by Aedes mosquitoes.1 Following infection, an individual remains vulnerable to re-infection with a different serotype of the virus. Clinically-apparent disease usually occurs with the first or second infections, rarely with the third or fourth.2 There is a wide spectrum of clinical manifestations from asymptomatic to undifferentiated fever, dengue fever (DF), dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS).3

With an estimated 50 million infections annually,3 the burden of dengue is a heavy one indeed,4 especially to countries in the Asia Pacific region.5 Despite sustained vector control efforts, Singapore has also not been spared from the disease. Although the Aedes premises index (percentage of premises found breeding Aedes mosquitoes) has been consistently maintained at between 1% and 2% since the 1980s, Singapore still experienced successive dengue outbreaks at intervals of five to seven years.6–10

In 2005, Singapore experienced its largest dengue outbreak on record.10 Only two years thereafter, another outbreak ensued. As this was not in keeping with the five-to-seven-year cycles previously experienced, we undertook epidemiological, entomological and virological studies to investigate the features of the 2007 dengue outbreak, and compared them with those of 2005, to determine the factors that triggered the outbreak.

METHODS
Dengue surveillance and control in Singapore

In Singapore, the Ministry of Health is responsible for the epidemiological surveillance and clinical management of dengue. The National Environment Agency (NEA),
Ministry of Environment and Water Resources takes charge of vector surveillance, control and research.

**Notification**

All medical practitioners are required by the Infectious Diseases Act to report all clinically-diagnosed and laboratory-confirmed dengue cases and deaths to the Ministry of Health by facsimile or by online electronic notification within 24 hours. They also are required to report cases that were initially diagnosed as DF but that later satisfied criteria for DHF. Directors of clinical laboratories also are mandated to notify the Ministry of Health whenever any blood sample provides evidence of recent dengue infection. Laboratory tests used in Singapore are RT-PCR, immunochromatographic assays, and commercial kits for the detection of NS1 or anti-DENV IgM. Epidemiological data routinely collected included name, identification number, age, ethnicity, gender, occupation, residential and workplace/school addresses and date of onset of illness.

**Vector control**

On receipt of notification, epidemiological data are immediately transmitted to the NEA, which undertakes field epidemiological investigations if necessary. All reported cases and breeding habitats are plotted, using a geographical information system, to determine clustering of cases and to identify high-risk areas for priority vector control.

**Serotype surveillance**

The Environmental Health Institute (EHI) at the NEA, monitors the circulating DENV serotypes and genotypes using samples submitted by Tan Tock Seng Hospital and by a network of sentinel private medical practitioners. Detection of dengue virus RNA and serotyping was performed with an in-house real-time PCR. Phylogenetic analyses of the dengue virus envelope protein gene has been described elsewhere. Serotyping of dengue virus was also carried out at the Department of Pathology, Singapore General Hospital, National University Hospital and Kandang Kerbau Hospital.

**Data analysis**

Only laboratory-confirmed cases reported to the Ministry of Health were included in the analysis reported here; we further restricted these cases to those who were Singaporean citizens or permanent residents. All duplicate notifications were removed before analysis. Cases with a history of travel within seven days before the onset of illness to countries where dengue also occurred were classified as imported and were not included in the analysis. A cluster was defined as two or more cases within a 150 meter radius (based on residential or workplace/school addresses) and with the onset of illness within a 14-day period. Denominators for the calculation of incidence rates were based on the estimated mid-year population obtained from the Singapore Department of Statistics, Ministry of Trade and Industry.

**Seroprevalence survey**

To determine the proportion of asymptomatic infections, voluntary blood sampling was carried out in 2007 in the three largest clusters of cases at Bukit Batok, Woodlands and Pasir Ris, where all household members residing in each site were invited to participate. A recruitment and sampling site was set up within each of the clusters to take blood samples (3 ml) and to conduct face-to-face interviews. Only residents who gave written consent were interviewed. Individuals whose serum samples contained anti-DENV IgM were scored as having a recent infection and those whose serum samples contained anti-DENV IgM but could not recall any recent symptoms of dengue infection were classified as asymptomatic.

**Statistical analysis**

Microsoft Office Excel 2007 and SPSS 15.0 were used for statistical analyses. Differences between the age-gender-standardized incidence rates were computed and tested for statistical significance using the Z-test. Statistical significance was taken at $P < 0.05$ level.

**Ethics**

The study was conducted primarily as part of a national public health programme, with supplemental data obtained from a community seroprevalence study which had been approved by the National Environment Agency Bioethics Review Committee (IRB 005.2) in 2007.

**RESULTS**

**Epidemiological findings**

A total of 8826 laboratory-confirmed cases of dengue were reported in 2007, an incidence rate of 192.3 per 100 000 population. Of these, 8637 (97.9%) were DF and 189 (2.1%) were DHF. Twenty-four fatalities were
reported in 2007, comprised of eight DF and 16 DHF cases, a case-fatality rate (CFR) of 0.27% for all dengue cases and 8.5% for all DHF cases, comparable to the outbreak in 2005. In 2005, 27 fatalities were reported, comprising three DF and 24 DHF cases, a CFR of 0.19% for all dengue cases and 6.1% for all DHF cases. The outbreaks in 2005 and 2007 differed in that 257 cases of DF/DHF were reported in January 2007, far fewer than the 1262 cases reported in the same period of 2005. Most cases (1633) were reported in July 2007, two months earlier than the peak of 2770 cases that were reported in September 2005 (Figure 1).

The median age of DF/DHF cases among Singapore residents in 2007 was 37 years (interquartile range 25 to 50), with a range from two days to 101 years, higher than the median age of 31 years (interquartile range 20 to 42), with a range from four days to 98 years, in 2005. The age-specific incidence rate for dengue was highest in the age group 55 years and above in 2007. In 2005, it was highest in the 15 to 24-year-old age group (Table 1).

The incidence in males was significantly higher than in females (209.3 per 100 000 and 150.3 per 100 000, respectively) and that was true for all ethnic groups ($P < 0.01$). Among Singapore residents in 2007, the age-gender-adjusted incidence rate of DF/DHF was highest in the Chinese (172.3 per 100 000) ($P < 0.01$), followed by the Malays (146.9 per 100 000) ($P < 0.05$) and the Indians (120.9 per 100 000). Among Singapore residents in 2005, the age-gender-adjusted incidence rate of DF/DHF was also highest in the Chinese (312.8 per 100 000) followed by the Malays (288.4 per 100 000) and the Indians (173.9 per 100 000).

The incidence rate in 2007 was highest among those residing in private condominiums (453.8 per

Table 1. Age-specific incidence rates of reported indigenous cases of dengue, Singapore, 2005 and 2007

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>2005</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number (%)</td>
<td>Incidence rate (per 100 000)</td>
</tr>
<tr>
<td>0–4</td>
<td>184 (1.3)</td>
<td>86.9</td>
</tr>
<tr>
<td>5–14</td>
<td>1 749 (12.5)</td>
<td>334.3</td>
</tr>
<tr>
<td>15–24</td>
<td>3 078 (21.9)</td>
<td>474.3</td>
</tr>
<tr>
<td>25–34</td>
<td>3 253 (23.2)</td>
<td>376.8</td>
</tr>
<tr>
<td>35–44</td>
<td>2 762 (19.7)</td>
<td>362.8</td>
</tr>
<tr>
<td>45–54</td>
<td>1 587 (11.3)</td>
<td>262.1</td>
</tr>
<tr>
<td>55+</td>
<td>1 419 (10.1)</td>
<td>217.7</td>
</tr>
<tr>
<td>Total</td>
<td>14 032 (100.0)</td>
<td>328.9</td>
</tr>
</tbody>
</table>
100 000), and was 1.3 times that of those residing in compound houses (351.1 per 100 000) and almost three times that of those residing in high-rise public housing apartments (156.5 per 100 000). This was different from 2005 when the lowest rate (298.8 per 100 000) was found in residents of private condominiums, while the incidence rate of those residing in compound houses was 710.7 per 100 000, and 332.1 per 100 000 for those living in high-rise public housing apartments.10

Cases were concentrated in the urban and suburban centres of the central (29.0%) and south-eastern (20.4%) parts of Singapore, with further geographical extension to the western suburban areas (Figure 2). A total of 3877 cases from 949 clusters (median three cases, range two to 117 cases) were identified. The total number of cases from reported clusters constituted less than half (46.8%) of all reported cases.

The largest clusters were at Bukit Batok (117 cases, July to September), Pasir Ris (71 cases, May to July) and Woodlands (67 cases, July to August). Two of these localities (Woodlands and Bukit Batok) also were affected in 2005, but with fewer cases.10 The seroprevalence study involving 1708 residents conducted in these three localities revealed that 3.3% (n = 56) had recent dengue infections. Among these residents with recent infection, 73.2%, ranging from 57.1% at Woodlands to 81.8% at Pasir Ris, did not recall any symptoms within the previous three months.

Virological findings
All four dengue virus serotypes circulated in Singapore from 2005 to 2007. The predominant serotype circulating in 2005 was DENV-1,10 but in January 2007 it was overtaken by DENV-2, which re-emerged with a clade replacement,14 and has since remained the predominant serotype (Figure 3). In 2007, RNA from 1044 confirmed cases of acute dengue infection were serotyped at the EHI, NEA, Department of Pathology, Singapore General Hospital and the laboratories at Tan Tock Seng Hospital and National University Hospital, and comprised 88.3% DENV-2, 6.4% DENV-1, 4.6% DENV-3 and 0.7% DENV-4.

Entomological findings
As in 2005, the distribution of dengue cases in 2007 was more closely associated with Aedes aegypti than with Aedes albopictus breeding sites (Figure 2).10 The overall Aedes premises index was 0.68% in 2007, lower than the 1.15% observed in 2005.10

The top three breeding habitats for Aedes aegypti in 2005 and 2007 were similar, with domestic containers (26% in 2005, 32% in 2007), ornamental containers (24% in 2005, 21% in 2007) and flower pot plates (7% in 2005, 11% in 2007) constituting more than half of all breeding habitats.10 However, for Aedes albopictus, there was a decrease in the number of breeding sites found in discarded receptacles (from 21% in 2005 to 4% in 2007).10

DISCUSSION
With the exception of median age of the cases, and the predominant dengue serotype, the epidemiological features of the 2007 epidemic were largely similar to those of 2005. The increase in median age and the
finding that those aged more than 55 years had the highest incidence are poorly understood. It is interesting to note that this phenomenon has accompanied the switch to DENV-2, and both the phenomenon and predominance of DENV-2 have persisted till 2010.

After the 2005 outbreak, the dengue control system was enhanced going into 2007. First, manpower that routinely carried out *Aedes* surveillance and source reduction was increased from 250 in 2005 to about 500 in 2007. On average, 116,764 residential premises and 3,011 non-residential premises (e.g. construction sites, schools) were inspected every month in 2007, resulting in almost all premises being inspected within the year. Second, an intensive source reduction exercise was conducted by NEA officers two to three months before the expected dengue season, to remove breeding and potential breeding grounds. Third, early warnings systems were developed through virological surveillance and ambient temperature monitoring, providing temporal risk stratification. Lastly, qualitative spatial risk stratification was performed using case, virus and larva surveillance data, to guide the deployment of staff. Despite the enhanced vector control which led to a premises index of 0.68%, which was significantly lower than the 2.24%, 1.7% and 2% found from 2002 to 2004 (when the same cosmopolitan genotype DENV was predominant), respectively, an outbreak still ensued.

Phylogenetic analyses of DENV-2 envelope gene sequences at EHI, NEA, revealed that the switch in predominant serotype in early 2007 coincided with a clade replacement within DENV-2. Within the Cosmopolitan genotype of DENV-2, there were two distinct subclades with strong temporal topology. The old clade was detected from 2000 to 2005 and the new clade from 2007 to 2008. The role of the small genetic changes between the two clades, in viral fitness, is being investigated. A similar observation was reported in Cuba, where the authors hypothesized that the 1997 severe outbreak in Cuba was a result of a small mutation that improved the fitness of DENV-2.

The epidemiology of dengue in Singapore has evolved from a paediatric problem in the 1960s to an adult infection since the 1980s. The median age has shifted from 14 years in 1973, to 37 years in 2007. This has been attributed to the lower transmission rate, which was demonstrated by a mathematical model that showed a declining trend in the force of infection (defined as per capita rate at which susceptible individuals in the community acquire infection) since the nationwide vector control programme was first implemented in the late 1960s.

Previous studies have demonstrated that more than 90% of dengue infections were asymptomatic. In a survey representative of the adult general population...
conducted in 2004, the prevalence of asymptomatic infections was found to be 95%. The prevalence of asymptomatic dengue infections in surveys conducted during the 2007 outbreak in three public housing estates ranged from 57.1% to 81.8%. The differences could be due to different methodologies.

A limitation on this study would be the reliance on notification data. The incidence rate is actually the case notification/detection rate. Although medical practitioners and directors of clinical laboratories were required to report all cases of DF/DHF to the Ministry of Health, mild cases with undifferentiated fevers may not seek medical care and so may not be reported. The actual incidence of dengue infection in 2007, therefore, could be higher than was reported. A limitation of the seroprevalence survey was that convenience sampling was done, and data collected may not be representative of the population. Nevertheless, it gives us an idea of the prevalence of asymptomatic infections in these outbreak areas.

The 2007 dengue epidemic in Singapore demonstrated the dynamic interactions of the virus, human host, vector and the environment, as evidenced by the resurgence caused by introduction of a new clade of DENV-2, despite sustained vector control efforts. Given the large estimated proportion of asymptomatic infections, the real extent of the problem could be much larger than what is currently known. Singapore remains vulnerable to major outbreaks of dengue through the constant introduction of viruses from travellers, and through local evolution of the virus.

Conflicts of interest
None declared.

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References:


Surveillance of hospitalizations with pandemic A(H1N1) 2009 influenza infection in Queensland, Australia

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Objective: To describe the demographic and clinical characteristics of patients hospitalized with pandemic A(H1N1) 2009 infection in Queensland, Australia between 25 May and 3 October 2009 and to examine the relationship between timing of antiviral treatment and severity of illness.

Method: Using data from the Queensland Health EpiLog information system, descriptive analysis and logistic regression modelling were used to describe and model factors which influence patient outcomes (death, admission to intensive care unit and/or special care unit). Data on patients admitted to hospital in Queensland with confirmed pandemic A(H1N1) 2009 infection were included in this analysis.

Results: 1236 patients with pandemic A(H1N1) 2009 infection were admitted to hospitals in Queensland during the study period. Of the total group: 15% were admitted to an intensive care unit or special care unit; 3% died; 34% were under the age of 18 years and 8% were 65 years of age or older; and 55% had at least one underlying medical condition. Among the 842 patients for whom data were available regarding the use of antiviral drugs, antiviral treatment was initiated in 737 (87.5%) patients, treatment commenced at a median of one day (range 1–33 days) after onset of illness. Admission to an intensive care unit or special care unit (ICU/SCU) or death was significantly associated with increased age, lack of timeliness of antiviral treatment, chronic renal disease and morbid obesity.

Discussion: Early antiviral treatment was significantly associated with lower likelihood of ICU/SCU admission or death. Early antiviral treatment for influenza cases may therefore have important public health implications.

The first case of pandemic A(H1N1) 2009 influenza infection in Australia was reported in a 28-year-old female in Queensland on 9 May 2009. Queensland, along with other Australian states and territories, invested in intense public health efforts to manage and control the outbreak. Information on the clinical spectrum of pandemic A(H1N1) 2009 illness and factors associated with admission to hospital is scarce in Australia. Internationally, it had been reported that the majority of the early cases reported mild, influenza-like illnesses with fever and respiratory symptoms, but more severe infections have also occurred. Obesity, underlying health conditions and delayed neuraminidase inhibitor treatment were the major risk factors for a poor outcome of infection. Risk factors for poor clinical outcomes for pandemic A(H1N1) 2009 infection in Australia warrant further investigation to help clinicians identify patients at high risk of severe disease.

Several surveillance systems were used to monitor and evaluate the progression of the outbreak in Queensland. These systems initially focused on notification data from public health units and laboratories. However, as the pandemic progressed, hospitalization data became of paramount importance for health planners. A new state-wide hospital-based surveillance application, EpiLog, was developed to monitor real-time admissions of patients with pandemic A(H1N1) 2009 infection to all public hospitals in Queensland. Data were also received from major private hospitals. This allowed monitoring of the outbreak and its impact on the hospital system.

We present findings from a retrospective analysis of data collected by this new surveillance system. The aims of the analysis were to describe the demographic and clinical characteristics of patients hospitalized with pandemic A(H1N1) 2009 infection in Queensland (between 25 May and 3 October 2009) and to examine the relationship between timing of antiviral treatment and severity of illness.
METHODS AND DATA COLLECTION

The data for this analysis were extracted from EpiLog. This web-based application was developed in Queensland for the surveillance of patients admitted to public hospitals with suspected or confirmed pandemic A(H1N1) 2009 influenza infection. The same data elements were provided by major private hospitals using a purpose-designed Microsoft Excel spreadsheet.

Data elements entered into EpiLog included pandemic A(H1N1) 2009 influenza infection status, self-reported medical conditions (morbid obesity, pregnancy, immunocompromised status, diabetes, chronic respiratory disease, renal disease, and cardiac disease), time of antiviral treatment initiation and intubation or ventilation status. EpiLog is linked to the Hospital Based Clinical Information System (HBCIS) used in public hospitals, which stores data relating to patient demographics and hospital stay with a unique patient identifier. Patient demographic data, admission and discharge details and ward transfer details were updated in EpiLog via this interface.

Data were extracted from EpiLog for analysis and aggregated with data received from private hospitals. Data on patients with confirmed pandemic A(H1N1) 2009 influenza infection who were admitted to hospitals in Queensland between 25 May and 3 October 2009 were analysed. Admission to an intensive care unit (ICU) or a special care unit (SCU) was used as a proxy for severity of illness.

Statistical analysis

The proportion of ICU/SCU admissions among hospitalized patients with pandemic A(H1N1) 2009 infection was calculated. Univariate association of various factors were evaluated using descriptive statistical techniques. The association between ICU/SCU admission and patient characteristics (age, sex, indigenous status, underlying medical conditions and whether antiviral treatment was received) was evaluated using univariate logistic regression followed by multivariate forward stepwise logistic regression test.

To assess the predictive value of various factors, the area under the receiver-operating characteristic (ROC) curves was calculated. The ROC curve evaluates the ability of the full logistic regression model to discriminate patients admitted to ICU/SCU from those with no ICU/SCU admission. The SPSS package (Version 12) was used for all analyses.

Ethical clearance was not required for this analysis. This analysis was conducted as a clinical audit (during a public health emergency event), required under the Health Services Act (1991).

RESULTS

Patient characteristics

There were 1236 hospitalized patients recorded in Queensland with confirmed pandemic A(H1N1) 2009 infection between 25 May and 3 October 2009. Table 1 summarizes selected demographic and clinical characteristics of these patients. The median age was 29 years (range, less than 1 month to 90 years). Eighty-four patients (7%) were less than one year of age, 420 (34%) were under 18 years of age and 96 (8%) were aged 65 years or over. Of the total study sample, 686 (55%) were recorded as having at least one underlying medical condition and 162 (13%) had at least two such conditions. A total of 80 patients were indigenous.

Antiviral drug administration data were available for 842 patients, with 703 (83%) recorded as receiving oseltamivir, 9 (1%) zanamivir and 25 (3%) treated with an unspecified antiviral and 105 (13%) as not having received any antiviral drugs. The median time from the onset of illness to the initiation of antiviral therapy was one day (range, less than 1 day to 33 days). Among patients for whom data on antiviral therapy timing were available (842), 561 (67%) received antiviral treatment within 48 hours of the onset of symptoms.

Intensive care unit and special care unit admissions and mortality

Patients admitted to ICU/SCU represented 189 of the 1236 (15%) patients. The median age was 49 years (range, 1 to 84 years). Patients who were admitted to ICU or SCU were more likely to be older, have diabetes or chronic cardiac or renal disease, be morbidly obese and not have received antiviral treatment within 48 hours of...
disease onset compared to those that were not admitted to ICU or SCU (Table 2). The median time from the onset of illness to the initiation of antiviral therapy was 3 days (range, zero to 28 days) for patients admitted to ICU or SCU. Among patients who were admitted to ICU or SCU, 12% (67/189) received antiviral drugs within 48 hours of the onset of illness. There was no significant difference in the proportion of indigenous and non-indigenous patients admitted to ICU or SCU.

Forty-one patients (3%) hospitalized with pandemic (H1N1) 2009 infection died. The median age of patients who died was 51 years (range 13 to 84 years); the median time from the onset of illness to death was
within 48 hours of onset. When these variables were included in a single model adjusting for each other, all factors remained significant except for chronic cardiac disease. Compared to patients who had received antiviral treatment within 48 hours of onset, patients who had not received antiviral drugs or received antiviral treatment later than 48 hours of onset were twice as likely to be admitted to ICU or SCU. A ROC curve was developed from the fitted predicted value from the final logistic regression model. The area under the operator characteristic curve was 0.76.

**DISCUSSION**

Using data from a newly established hospitalisation surveillance system, we examined the epidemiological profile of 1236 patients admitted to hospitals in Queensland, Australia with confirmed pandemic A(H1N1) 2009 infection. We found that 34% of the hospitalized patients were under the age of 18 years, more than one third were between the ages of 18 and 49 years, and only 8% were 65 years of age or older. This pattern is similar to results reported elsewhere.4–6

Pregnancy has been associated with increased hospitalization and severity of illness due to pandemic

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**Table 3. Multivariate analysis of factors associated with admission to ICU or SCU in hospitalized patients with confirmed pandemic A(H1N1) 2009 infection, Queensland, Australia (May to October 2009)**

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
</tr>
<tr>
<td>Less than 10</td>
<td>0.1 (0.1–0.7)</td>
</tr>
<tr>
<td>10–17</td>
<td>1</td>
</tr>
<tr>
<td>18–44</td>
<td>3.9 (1.4–11.2)</td>
</tr>
<tr>
<td>45–64</td>
<td>7.1 (2.6–21.3)</td>
</tr>
<tr>
<td>65+</td>
<td>5.7 (1.8–18.2)</td>
</tr>
<tr>
<td><strong>Antiviral treatment initiated within 48 hours of onset</strong></td>
<td></td>
</tr>
<tr>
<td>Yes†</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>2.1 (1.34–3.3)</td>
</tr>
<tr>
<td><strong>Chronic renal disease</strong></td>
<td></td>
</tr>
<tr>
<td>No†</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>2.7 (1.3–5.7)</td>
</tr>
<tr>
<td><strong>Morbid obesity</strong></td>
<td></td>
</tr>
<tr>
<td>No†</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>1.9 (1.4–3.6)</td>
</tr>
</tbody>
</table>

* Odds Ratio and 95% Confidence Interval; † Reference group

14 days (range 1 to 68 days) and 27 (67%) had an underlying medical condition. Of the patients who died, 80% had received antiviral drugs. Among the patients who died who received antiviral treatment, the median time from the onset of illness to the initiation of antiviral therapy was 3 days (range, less than 1 day to 28 days). Forty-eight per cent of those who died received antiviral therapy within 48 hours of the onset of symptoms.

Patients with any severe outcome (defined as those admitted to an ICU or SCU plus those who died) were older (median age 50 years, range from less than 1 to 85) and had a longer median time (4 days, range between less than 1 day to 28 days) between onset of illness and the initiation of antiviral therapy, compared to other hospitalized patients, in whom the median age was 30 years (range from less than 1 to 90) and the median time between onset and receiving antiviral drugs was 1 day (range from less than 1 day to 33 days).

**Tables 2 and 3** show the univariate and multivariate results of the logistic regression analysis. In the unadjusted model, factors significantly associated with increased likelihood of admission to ICU or SCU were older age, chronic renal disease, chronic cardiac disease, morbid obesity and not receiving antiviral treatment within 48 hours of onset. When these variables were included in a single model adjusting for each other, all factors remained significant except for chronic cardiac disease. Compared to patients who had received antiviral treatment within 48 hours of onset, patients who had not received antiviral drugs or received antiviral treatment later than 48 hours of onset were twice as likely to be admitted to ICU or SCU. A ROC curve was developed from the fitted predicted value from the final logistic regression model. The area under the operator characteristic curve was 0.76.
In our study, 7% of hospitalized patients with confirmed pandemic A(H1N1) 2009 infection were pregnant compared to the 1% prevalence of pregnancy in the general population. Although a slightly higher proportion of pregnant patients were admitted to ICU or SCU, this did not reach statistical significance.

We found that morbid obesity and chronic renal disease were associated with increased odds of admission to ICU or SCU. Morbid obesity has been associated with increased severity of illness due to pandemic A(H1N1) 2009 infection in previous studies. Similarly, chronic renal disease has also been reported as a potential risk factor for severity of illness due to pandemic A(H1N1) 2009 infection.

Considerably higher rates of hospital admission due to pandemic A(H1N1) 2009 influenza infection have been reported among indigenous people in other Australian states, New Zealand and Canada compared to those of European descent. This is possibly due to a higher prevalence of medical risk factors, poorer access to primary health care services and socioeconomic factors in this community. However, we found that the proportion of hospitalized patients admitted to ICU or SCU was similar among indigenous and non-indigenous Queenslanders. Missing data from indigenous status may influence the proportion of hospital admission recorded as indigenous. Ten per cent of data on indigenous status was unknown or missing which limited our interpretation of the association between ICU/SCU admission and indigenous status.

Our final logistic regression model revealed that factors such as older age, initiation of antiviral treatment later than 48 hours and presence of morbid obesity and/or chronic renal disease were significantly associated with admission to ICU/SCU. This model had reasonable predictive accuracy for admission to ICU or SCU, with the area under the ROC curve being 0.76 (1 indicating perfect predictive accuracy and 0.5 no predictive accuracy above chance).

Our analysis has several limitations. Analysis was undertaken using only data on patients with laboratory-confirmed pandemic A(H1N1) 2009 infection. This may underestimate the true number of cases as some may not have been tested or have tested negative due to technical or timing factors. The data on underlying medical conditions were from patient self-report and were not clinically validated. Body mass index values were not recorded, so it is unclear what role clinical judgement may have played in categorization of morbid obesity (or other medical conditions for that matter). There is also the possibility of reporting bias, which may results in confounding in our logistic regression model. Despite the use of a standardized data collection template, not all information was captured for all cases and some data fields were incomplete. The study used data from two sources: EpiLog for public hospitals and separately submitted spreadsheets for private hospitals. It was not possible to verify the data recorded. Finally, as social-demographic data were collated by linking the EpiLog system and HBCIS missing data were unavoidable.

Despite these limitations, EpiLog provides an example of a new surveillance application that was rapidly developed to meet an urgent public health need. It enabled close to real-time monitoring of the severity of pandemic A(H1N1) 2009 infection and its impact on Queensland’s hospital system and critical care services. It was possible to monitor the progress of the pandemic and gain rapid information on risk factors for severe disease and patient outcomes. Reflection on the use of EpiLog during the 2009 influenza pandemic led to several enhancements of the application. Many of the improvements related to streamlining the interface between EpiLog and HBCIS and the efficient management of data quality and reporting issues.

Finally, there is growing evidence that early treatment with antiviral medication may reduce the likelihood of hospitalization and death due to pandemic A(H1N1) 2009 infection. Our study supports these findings. Patients admitted to an ICU or SCU, or who died, were less likely to have received antiviral therapy within 48 hours of the onset of symptoms compared to other hospitalized patients. Early antiviral treatment for influenza cases may therefore have important public health implications for example for reducing the severity of the impact of pandemic A(H1N1) 2009 infection.

Conflicts of interest
None declared.

Funding
None.
References:


Western Pacific Surveillance and Response
Instructions to Authors

Aim of Western Pacific Surveillance and Response
To create a platform for sharing information to improve surveillance of and response to public health events in the Western Pacific Region.

Objectives
- To produce a web-based publication on surveillance and response activities in the region that has high exposure and is freely accessible.
- To promote information sharing on experiences and lessons learnt in surveillance and response for public health events in the Western Pacific Region and globally.
- To build capacity in communicating epidemiological findings in the Western Pacific Region.
- To highlight new and relevant technical or guidance documents and meeting reports published by the World Health Organization, Western Pacific Regional Office.

Audience
Western Pacific Surveillance and Response (WPSAR) is aimed at people studying, conducting research or working in surveillance of and response to public health events both within the region and globally.

Scope
WPSAR covers all activities related to the surveillance of and response to public health events. Such activities may be implementation or evaluation of surveillance systems, investigations of public health events, risk assessments both in rapid responses and policy development, outbreak investigations and research on routine public health activities. Public health events may be in any of the following areas: communicable diseases, natural disasters, bioterrorism and chemical and radiological events.

Frequency
Journal articles will be published an article at a time building up to an issue every quarter. This means that articles will be uploaded onto the website after the review and editing process therefore allowing timely dissemination. Printed copies of the journal are available for areas with limited internet access on request after the end of each quarter.

Instructions to authors for manuscript writing and submission
WPSAR follows the guidelines from the Uniform Requirements for Manuscripts Submitted to Biomedical Journals by the International Committee for Medical Journal Editors (ICMJE, http://www.icmje.org/).

Format for Manuscripts
Please submit all articles in double spaced 12 point Arial font in a Microsoft® Office Word file or a compatible file in English.

The format of the article will depend on the type. There are letters to the editor, perspectives, case reports/case series, lessons from the field, surveillance reports, surveillance system implementation/evaluation, risk assessments, original research, news items and meeting/conference reports.

Letters to the Editor
A letter commenting on a previously published article OR a letter commenting on the theme of the issue.
- Word limit: ≤500 words
- ≤5 references
- ≤1 illustration

Perspectives
An unstructured article discussing an issue regarding surveillance of and response to public health events. The scope of the discussion must be clearly defined.
  - Word limit: ≤1000 words
  - ≤10 references
  - ≤1 illustration

Case Report/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: ≤2000 words
  - ≤15 references
  - ≤3 figures/graphs/pictures

Lessons from the Field
An article describing an issue faced in field epidemiology and the experience in trying to overcome the issue.
  - Structured article with an abstract of ≤250 words and sections for problem, context, action, outcome and discussion
  - The abstract should also be structured with problem, context, action, outcome, and discussion
  - Word limit: ≤2000 words
  - ≤15 references
  - ≤3 figures/graphs/pictures

Surveillance Reports
An article of a summary and interpretation of surveillance data for a given period of time. A description of the surveillance system and the limitations of the data collected must be included.
  - Unstructured abstract of ≤250 words
  - Word limit: ≤2000 words
  - ≤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: ≤2000 words
  - ≤15 references
  - ≤3 figures/graphs/pictures

Risk Assessments
An article detailing a risk assessment of a public health threat or event. The risk assessment may be planned and formal or rapid and informal. The scope and methods of the risk assessment must be clearly defined.
  - Structured article with an abstract of ≤250 words, introduction, methods, results and discussion
  - The abstract should also be structured with objective, methods, results, and discussion
  - Word limit: ≤2000 words
  - ≤15 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, introduction, methods, results and discussion
- The abstract should also be structured with introduction, methods, results, discussion
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News items and meeting and conference reports will not undergo peer review. Please contact the Editor at WPSAR@wpro.who.int if you intend on submitting such an article.

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Refer to the article type for the limit on illustrations (graphs, tables or diagrams). Please insert all illustrations at the end of the manuscript with a title. The illustration must be referred to in the text and must be able to 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 for illustrations should have superscript letters assigned and an explanation provided below the illustration.

References

Reference the most recent and relevant publications. Please use Vancouver style referencing. Sample references can be viewed online:http://www.nlm.nih.gov/bsd/uniform_requirements.html.

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

These results are consistent with the original study.11

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

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Every article will be reviewed firstly by the editorial team to ensure the article is within the scope of WPSAR and the quality is sufficient for undergoing peer review. All articles with the exception of news items and meeting and conference reports will undergo external peer review by two reviewers. This will be a blinded peer review process where the reviewer does not know the identity of the author(s) and the author(s) do not know the identity of the reviewer. Author(s) may be asked to revise the manuscript as a result of the peer review. After satisfactory revision, accepted manuscripts will be edited and sent to the author(s) for final approval before publication.

Authorship

All authors should have contributed significantly to the article through one or more of the following in each category A, B and C:

A
- Study design
- Data collection
- Data analysis
- Data interpretation
- Writing the article

B
- Drafting the manuscript
- Critically revising the manuscript

C
- Final approval of the manuscript for submission

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