

Results: We followed 13,115 children for 284,501 child-weeks and identified 65 case-patients hospitalized with severe acute respiratory infections. The median age of the case-patients was 8.5 months (interquartile range, IQR 3–15) and 44 (68%) were male. Case-patients were admitted a median of 2 days (IQR 1–3) after symptoms onset and were hospitalized for 4 days (IQR 3–6). Viruses were detected in specimens from 34 (52%) case-patients; RSV in 25 (74%), HPIV3 in 6 (15%), influenza A viruses in 2 (6%), influenza B virus in 2 (6%), and adenoviruses in 2 (6%) specimens. The overall incidence rate of hospitalization associated with a respiratory virus was 12/100,000 child-weeks. RSV was associated with 8.8 hospitalizations per 100,000 child-weeks, HPIV3 with 2.1/100,000 child-weeks, influenza viruses with 1.4/100,000 child-weeks, and adenoviruses with 0.7/100,000 child-weeks.

Conclusion: Respiratory viruses, and in particular RSV, were commonly associated with hospitalization for severe acute respiratory infection among children in this rural setting during June–October. In the absence of affordable and effective RSV specific interventions, other strategies like handwashing and respiratory hygiene should be explored as scalable prevention strategies in low-income settings.

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The epidemiology of pneumonia in a birth cohort of children living on the Thai–Myanmar border

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Background: There are an estimated 150 million episodes of childhood pneumonia per year resulting in up to 20 million hospital admissions and 1.9 million deaths, making pneumonia the commonest cause of death in children under-five. In order to tackle this huge global health problem robust regionally specific pneumonia epidemiology data must be known.

Methods: We did a longitudinal birth cohort study based in Maela camp for displaced persons on the Thai–Myanmar border. 999 mothers were enrolled during pregnancy and their infants followed from birth until 2 years of age. As well as routine monthly visits the mothers were asked to bring their child to the clinic during an illness. Pneumonia was diagnosed using the WHO criteria. All children with pneumonia had a complete blood count, C-reactive protein (CRP), nasopharyngeal aspirate (NPA) and chest x-ray (CXR) performed. Chest x-rays were interpreted using the WHO standardised method. PCR was performed to detect respiratory syncytial virus (RSV), adenovirus, Influenza A, influenza B and human metapneumovirus.

Results: There were 1,085 clinical episodes of pneumonia over 1,495 child-years of observation, giving an incidence rate of 0.73 episodes/child-year. The incidence of CXR primary endpoint pneumonia (PEP) was 0.22 episodes/child year and was more commonly found in children >1 year ($p < 0.001$). PEP was also associated with

a neutrophil count $>7.5 \times 10^9/L$ and a CRP $\geq 40 \text{ mg/L}$ (OR 2.41; $p < 0.001$).

A virus was detected in 61.3% of pneumonia episodes, most commonly RSV. Adjusting for age, RSV was associated with more severe clinical disease (OR 2.18; $p = 0.007$) and the presence of other infiltrate on CXR ($p = 0.001$).

Using a multivariate model, having a mother <18 years ($p = 0.001$) and a small volume of living space per person ($p = 0.03$) were found to be risk factors for pneumonia. Distance to next house ($p = 0.04$) was a risk factor for multiple episodes of pneumonia and distance from stove to the infants bed ($p = 0.03$) was a risk factor for PEP.

Conclusion: The study demonstrated a high incidence of pneumonia in this population with a particularly large burden of viral-associated infections. Important risk factors for developing pneumonia were both maternal and infant age and also living conditions.

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Spatial and temporal dynamics of dengue in southern Vietnam

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Background: Dengue epidemics of variable magnitude and geographic distribution occur annually in southern Vietnam. Detailed analyses of spatial and temporal trends may further our understanding of the underlying determinants of dengue transmission dynamics, and may help to improve tools for predicting the timing and magnitude of dengue epidemics.

Methods: We analysed a monthly time series of hospitalized dengue cases reported to the Vietnamese national dengue surveillance program from the southern 19 provinces of Vietnam, from 2001 – 2010. Wavelet analysis was used to explore the periodicity in dengue incidence. Differences in the phase of annual cycles were calculated to investigate the synchrony of dengue epidemics between provinces and districts, and the association between dengue and climatic factors. We used a linear model to quantify the relationship between dengue incidence during the inter-epidemic period and the magnitude of the following epidemic.

Results: Between 2001 and 2010, a total of 592,938 dengue cases were reported from the southern 19 provinces of Vietnam, corresponding to a median annual incidence of 232 cases per 100,000 population (annual range 78 – 288/100,000, and range by province and year 5 – 810/100,000). In terms of per capita incidence, substantially higher epidemic peaks were reached in provinces outside Ho Chi Minh City than in the city itself. The annual peak occurred consistently later in HCMC (~2 months) than in other provinces, and annual epidemics were initiated in multiple and variable locations. Wavelet analysis identified a strong annual periodicity, but a less marked multi-annual cycle. The incidence of dengue during annual epidemics (April – December) was significantly positively

correlated with the incidence during the preceding inter-epidemic period (January – March; $p < 0.001$, $r^2 = 0.62$).

Conclusion: As in other settings, the dynamics of dengue in southern Vietnam are characterized by spatial and temporal heterogeneity. Although the greatest absolute number of cases occurred in the highly urban setting of HCMC, substantially higher per capita incidence was reached during periodic epidemics in other more rural provinces. The factors underlying this, and the observed consistent lag to the seasonal epidemic in HCMC, are not clear but may include differences in population immunity and/or vector to human density ratios.

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Dengue attack rate and proportion of asymptomatic infections in the Kampong Cham prospective community study, 2011: preliminary data

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Background: Dengue fever is a major public health problem in Cambodia (estimated 2010 pop. 14 million). All four dengue virus serotypes have circulated in the country during the past 5 years. Annual incidence of symptomatic dengue virus infection has been reported at 2 per 1000 for persons <16 years of age and the breakdown of cases with DSS or DHF is unclear. As all await a dengue vaccine, the target vaccination levels will depend on the force of transmission and the proportion of asymptomatic dengue infections.

Methods: In 2011, the Institut Pasteur du Cambodge (IPC) and the Dengue National Control Program with support from US Naval Medical Research Unit #2 (NAMRU-2) undertook a community-based prospective study for dengue in 14 villages in rural Kampong Cham province. Suspect (febrile) cases were tested by real-time RT-PCR, NS1 antigen detection kit, anti-DENV IgM and IgG serologies. Biologically-confirmed index cases were followed up by exhaustive household serosurveys within 200 meters around the index cases' residence.

Results: Between July 10 and 16 October 2011 (Monsoon), an average monthly population of 5,635 persons aged 6 months – 20 years agreed to be monitored weekly of which 1,365 presented fever and were tested for dengue. In all, 57 (4.2%) symptomatic dengue cases were identified by surveillance. One case developed fatal hemorrhagic dengue. In the investigations around 10 febrile index cases an additional 1,393 persons were tested for recent dengue infection. Among these, 40 cases were positive, of which 29 (72.5%) declared they had felt no symptoms. The overall symptomatic dengue attack rate was estimated at 12 per 1000 for the study period. Finally, one additional case of Japanese Encephalitis virus was identified. Analysis is ongoing.

Conclusion: Preliminary results show that dengue under-reporting is high in Cambodia. Furthermore, the majority of biologically-confirmed cases in systematic household investigations remain asymptomatic. These data must be included in mathematical models to estimate vaccine coverage needs.

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Surveillance and characterisation of influenza among patients with influenza-like illness in Bali, Indonesia

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Background: Indonesia is of key strategic importance for influenza surveillance and research, as it continues to report the majority of highly pathogenic avian influenza (H5N1) outbreaks worldwide. However, research on the ecology and evolution of influenza viruses in Indonesia has been severely limited. Within Indonesia, the island province of Bali in particular might be a hotspot for mixing of influenza viruses from different geographic regions and host species, due to high densities and close proximity of humans, poultry and pigs, along with its status a popular tourist destination.

Methods: The Molecular Epidemiology of Influenza A in Bali project (“BaliMEI”) aims to conduct five years of active surveillance and characterisation of influenza viruses among patients presenting with influenza-like illness at health facilities across Bali. Nasopharyngeal swabs are screened for Influenza A and B, and Influenza A-positive samples are subtyped and tested for genetic markers of resistance to oseltamivir, using PCR based assays. Sequencing and phylogenetic analysis of samples is planned to take place at a later stage.

Results: To date, we have tested 772 patients (mean age = 11y, range = <1 to 79y) across all nine districts of Bali who presented with influenza-like illness between July 2010 and December 2011. Of these, 142 (18.4%) tested positive for Influenza A, and 28 (3.6%) tested positive for Influenza B. Findings show strong temporal patterns in circulation of seasonal and pandemic influenza viruses, with influenza B dominating from July to September 2010, pandemic A/H1N1 in December 2010 to April 2011, and seasonal A/H3N2 in July to October 2011. Two human cases of highly pathogenic avian influenza H5N1 were also identified within Bali during the study period, both of which were fatal.

Conclusion: With the continued incidence and high fatality of H5N1 among humans in Indonesia, ongoing influenza surveillance is crucial. This project has collected a unique library of influenza isolates from Bali, which could give valuable insights into the ecology and evolution of influenza in the region. Further details on the methodologies, results, and lessons learned from the first two years of this study will be discussed.

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