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## **Paediatric Active Enhanced Disease Surveillance (PAEDS) annual report 2016: Prospective hospital- based surveillance for serious paediatric conditions**

Jocelyne E McRae, Helen E Quinn, Gemma L Saravanos, Alissa McMinn,  
Philip N Britton, Nicholas Wood, Helen Marshall and Kristine Macartney on behalf  
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# Paediatric Active Enhanced Disease Surveillance (PAEDS) annual report 2016: Prospective hospital-based surveillance for serious paediatric conditions

Jocelyne E McRae, Helen E Quinn, Gemma L Saravanos, Alissa McMinn, Philip N Britton, Nicholas Wood, Helen Marshall and Kristine Macartney on behalf of the PAEDS network

## Abstract

### Introduction

The Paediatric Active Enhanced Disease Surveillance (PAEDS) network is a hospital-based active surveillance system employing prospective case ascertainment for selected serious childhood conditions, particularly vaccine preventable diseases and potential adverse events following immunisation (AEFI). PAEDS data is used to better understand these conditions, inform policy and practice under the National Immunisation Program, and enable rapid public health responses for certain conditions of public health importance. PAEDS enhances data available from other Australian surveillance systems by providing prospective, detailed clinical and laboratory information on children with selected conditions. This is the third annual PAEDS report, and presents surveillance data for 2016.

### Methods

Specialist nurses screened hospital admissions, emergency department records, laboratory and other data, on a daily basis in 5 paediatric tertiary referral hospitals in New South Wales, Victoria, South Australia, Western Australia and Queensland to identify children with the conditions under surveillance. Retrospective data on some conditions was also captured by an additional hospital in the Northern Territory. Standardised protocols and case definitions were used across all sites. Conditions under surveillance in 2016 included acute flaccid paralysis (AFP) (a syndrome associated with poliovirus infection), acute childhood encephalitis (ACE), influenza, intussusception (IS; a potential AEFI with rotavirus vaccines), pertussis, varicella-zoster virus infection (varicella and herpes zoster), invasive meningococcal and invasive Group A streptococcus diseases. Most protocols restrict eligibility to hospitalisations; ED only presentations are also included for some conditions.

### Results

In 2016, there were 673 cases identified across all conditions under surveillance. Key outcomes of PAEDS included: contribution to national AFP surveillance to reach World Health Organization (WHO) reporting targets; identification of the leading infectious causes of acute encephalitis which included human parechovirus, influenza, enteroviruses, *Mycoplasma pneumoniae*, and bacterial

meningo-encephalitis; demonstration of high influenza activity with vaccine effectiveness (VE) analysis demonstrating some protection offered through vaccination. All IS cases associated with vaccine receipt were reported to the relevant state health department. Varicella and herpes zoster case numbers increased from previous years associated with suboptimal vaccination in up to 40% of cases identified. Pertussis surveillance continued in 2016 with the addition of test negative controls captured for estimating vaccine effectiveness. Surveillance for invasive meningococcal disease showed predominance for serotype B in absence of immunisation, and new invasive group A streptococcus surveillance captured severe disease in children.

## Conclusions

PAEDS continues to provide unique policy-relevant data on serious paediatric conditions using hospital-based sentinel surveillance.

Keywords: paediatric, surveillance, child, hospital, vaccine preventable diseases, adverse event following immunisation, acute flaccid paralysis, encephalitis, influenza, intussusception, pertussis, varicella zoster virus, meningococcal, group A streptococcus.

## Introduction

This is the third annual report of the Paediatric Active Enhanced Disease Surveillance (PAEDS) network and summarises data collected in 2016. Previous years PAEDS data can be found in the 2015 annual report<sup>1</sup> and historical data for 2007–2014, including impacts and outcomes, in the PAEDS 2014 inaugural report.<sup>2</sup>

PAEDS is a hospital-based active surveillance system for serious childhood conditions of public health importance, particularly vaccine preventable diseases (VPDs) and adverse events following immunisation (AEFI). PAEDS, through prospective case identification and ascertainment, collects timely and detailed clinical data on children requiring hospitalisation for the select conditions under surveillance. In some instances, emergency department (ED) presentations are also included. PAEDS data is used to better understand these conditions, inform policy and practice under the National Immunisation Program (NIP) and enable rapid public health responses for certain conditions of public health interest. PAEDS is well positioned compared to other passive surveillance programs that are usually less able to adequately capture such timely and comprehensive data.<sup>3</sup>

During 2016, the PAEDS network consisted of 6 participating hospitals: The Children's Hospital at Westmead (CHW), Sydney, New South Wales (NSW); Royal Children's Hospital (RCH), Melbourne, Victoria; Women's and Children's Hospital (WCH), Adelaide, South Australia; Princess Margaret Hospital (PMH), Perth, Western Australia; and Lady Cilento Children's Hospital (LCCH), Brisbane, Queensland. The sixth hospital: Royal Darwin Hospital (RDH), Darwin, Northern Territory joined PAEDS in early 2017 and participated in retrospective data collection from July 2016 on some conditions. PAEDS is coordinated by the National Centre for Immunisation Research and Surveillance (NCIRS) based at CHW in Sydney.

PAEDS activities are substantially supported through funding from the Australian Government Department of Health and the 6 participating states' health departments. In addition, the Australian Paediatric Surveillance Unit (APSU) and the Influenza Complications Alert Network (FluCAN) collaborate with PAEDS on specific conditions. PAEDS produces monthly data reports for all funding bodies and collaborators.

## Methods

### Active case ascertainment

Under PAEDS, specialist surveillance nurses in each hospital identified children diagnosed with the conditions under surveillance, as defined in Table 1, by reviewing admission and emergency department databases, clinical records, laboratory logs and through liaison with medical, laboratory and nursing staff.<sup>1,2</sup>

For 2016, all 6 of the PAEDS participating hospitals were approved by their respective Human Research Ethics Committees to operate under a waiver of consent model for surveillance of all conditions. Surveillance nurses collected detailed clinical information from the medical records and vaccination history from the Australian Childhood Immunisation Register (ACIR). Information not available in the medical record was obtained by contacting the child's parent/guardian; participation was voluntary. In some cases, the parent/guardian was approached for consent to their child's participation in additional research studies, involving elements such as long-term follow-up or non-routine specimen collection. In this instance, a patient information sheet and consent form was provided to facilitate participation (Figure 1).

### Conditions under surveillance

In 2016, there were 7 conditions under surveillance at all PAEDS sites: acute flaccid paralysis (AFP), acute childhood encephalitis (ACE), intussusception (IS), pertussis, and varicella-zoster virus infection (VZV; varicella and herpes zoster), with the addition of 2 new conditions commenced at all sites: invasive meningococcal disease (IMD) and invasive group A streptococcus (IGAS). Surveillance for influenza (in collaboration with FluCAN) was undertaken at 2 PAEDS sites: CHW (Sydney) and PMH (Perth). In addition, in 2016, data collected from surveillance of 2 PAEDS conditions in children aged <5 years, AFP and ACE, were analysed monthly

to identify any serious acute neurologic events (SANE) that occurred within 6 weeks of receipt of a seasonal influenza vaccine.

### Collection of biological samples

Surveillance nurses facilitated collection of samples in line with public health requirements and condition protocols. For example, children hospitalised with AFP require collection of 2 stool samples for enteric virus identification by the National Enterovirus Reference Laboratory (NERL) in Melbourne as part of the Global Polio Eradication Initiative.<sup>4,5</sup> For other conditions, samples were collected for virus genotyping (e.g. VZV) or for additional pathogen characterisation (e.g. ACE, IGAS).

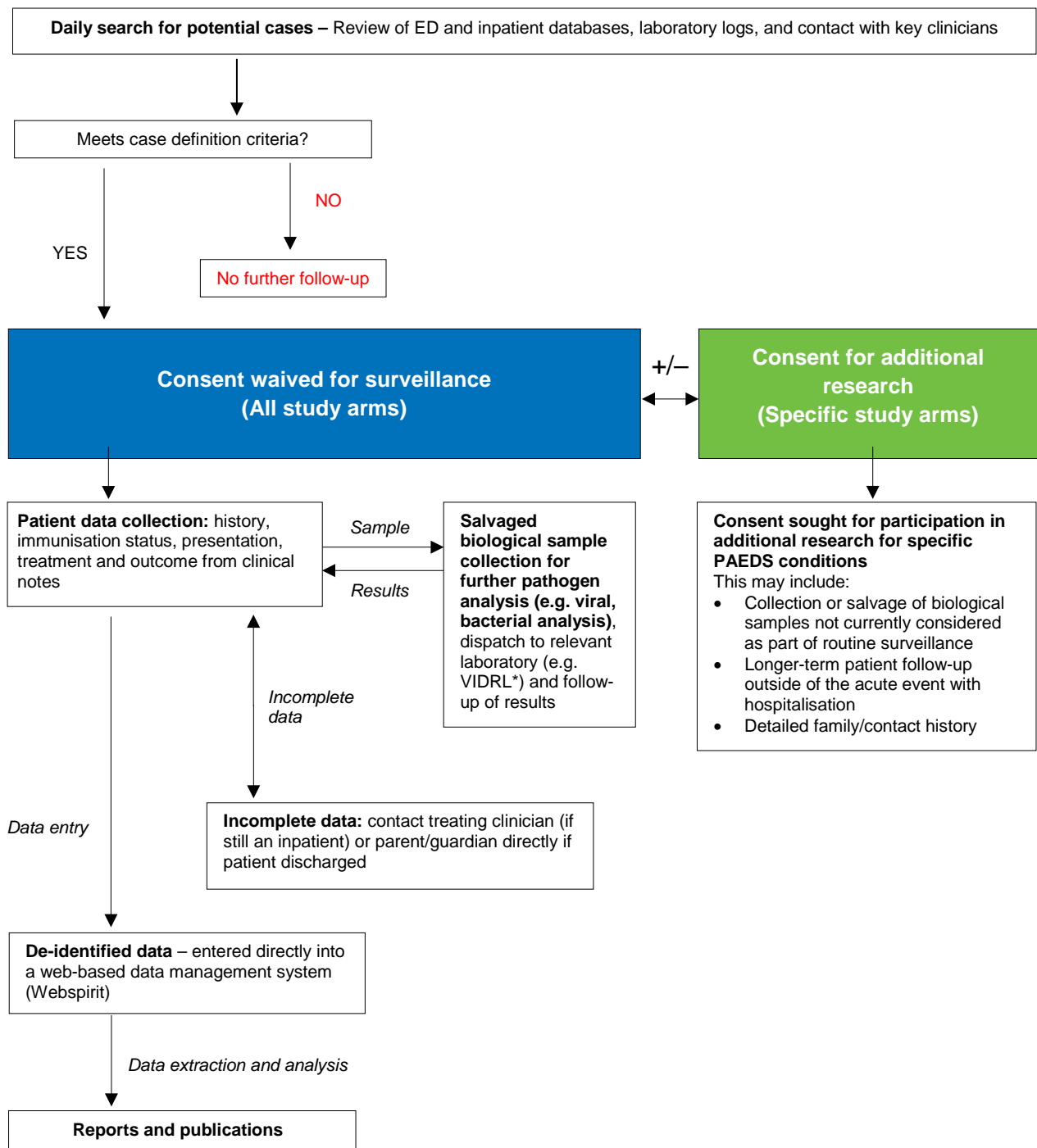
### Quality assurance and ICD-10-AM audits

To check for completeness of case ascertainment, PAEDS nurses at each site conducted regular retrospective audits of hospitalisation records by searching for primary and secondary ICD-10-AM codes ascribed to the relevant conditions (e.g. K56.1 for IS). Cases ascertained through these audits were compared with the cases ascertained prospectively by PAEDS for the same period. Additional cases identified by the ICD-10-AM audit process were retrospectively included into PAEDS. As an additional quality assurance measure, periodic audits were undertaken by investigators of case medical records to assess accuracy of data collected.

### Data management

PAEDS utilises a web-based data management system called 'WebSpirit'<sup>6</sup> which enables online data entry by surveillance nurses at each site and centralised data extraction. Data is held securely and exported on a regular basis by staff at the PAEDS coordinating centre for clinical review, monthly quality checks, analysis and reporting. Data for 2 specific study arms: FluCAN and IGAS are also recorded on a separate secure system, Redcap.

Figure 1: PAEDS method for surveillance using the waiver of consent model plus opt-in consent for additional research of specific study arms



\* VIDRL = Victorian Infectious Diseases Reference Laboratory

**Table 1: PAEDS conditions under surveillance, case definitions and rationale, 2016**

Condition and case definition	Rationale
<p><b>Acute flaccid paralysis (AFP)</b>  <i>Case definition:</i>                      Any child aged birth to &lt;15 years and presenting with acute flaccid paralysis: onset of flaccid paralysis in one or more limbs or acute onset of bulbar paralysis.</p>	<p>WHO requires active national surveillance for cases of AFP in children aged &lt;15 years in order to monitor for potential cases of paralytic poliomyelitis. PAEDS collaborates with the APSU in nationwide surveillance in an effort to meet the target enrolment of 1 non-polio AFP case / 100,000 children aged &lt;15 years per year. Data collected on AFP also contributes to separate analysis for SANE*.</p>
<p><b>Acute childhood encephalitis (ACE)</b>  <i>Case definition:</i>                      Any child aged birth to &lt;15 years <b>AND</b> hospitalised with acute encephalopathy <b>AND</b> who has <i>one or more</i> of the following: fever, seizures, focal neurological findings, at least one abnormality of cerebrospinal fluid, or EEG/neuroimaging findings consistent with infection-related encephalitis.</p>	<p>Encephalitis is a critical condition that is considered a marker syndrome for emerging infectious diseases. It is most often caused by viruses (including those which are or potentially will be vaccine preventable). It can also be immune-mediated, and uncommonly can be associated with vaccine receipt. As there is limited epidemiologic data on encephalitis, PAEDS is uniquely placed to undertake active, syndromic surveillance and can collect biological specimens. Enrolment of participants into comprehensive follow-up studies to improve understanding of long-term neuropsychological sequelae also occurs.<sup>7</sup> Data collected on ACE also contributes to separate analysis for SANE*.</p>
<p><b>Influenza – FluCAN (Seasonally: April–October)</b>  <i>Case definition:</i>                      Any child aged birth to &lt;18 years who is hospitalised, clinically suspected of having influenza (respiratory symptoms +/- fever) and confirmed influenza PCR-positive.</p>	<p>The emergence of H1N1-09 influenza in 2009 demonstrated the importance of enhanced influenza surveillance in children.<sup>8</sup> PAEDS provides unique timely sentinel data from 2 sites (Sydney and Perth) on influenza hospitalisations, including complications and deaths, which can be used to inform public health response and policy. The data on children supplements adult data from 15 other FluCAN sites. Information on influenza test-negative (control) patients with acute respiratory illness (ARI) is also collected and allows calculation of vaccine effectiveness to be performed.</p>
<p><b>Intussusception (IS)</b>  <i>Case definition:</i>                      Any child aged &lt;9 months presenting with a diagnosis of acute intussusception confirmed using the Brighton Collaboration clinical case definition (Level 1 or 2). Includes hospitalised or ED only.<sup>9</sup></p>	<p>Intussusception is the most common cause of bowel obstruction in infants and young children and was associated with a previous rotavirus vaccine in the USA which was withdrawn in 1999. Timely, active and systematic surveillance of IS cases is important and has identified a temporal but low incidence association with the rotavirus vaccines currently available under the NIP (since July 2007).<sup>10</sup> Surveillance also aims to describe the epidemiology, aetiology and severity of IS.<sup>11,12</sup></p>
<p><b>Pertussis</b>  <i>Case definition:</i>  <u>Hospitalised pertussis</u> - Any child aged birth to &lt;15 years hospitalised with laboratory confirmed pertussis.  <u>Pertussis vaccine effectiveness study</u> – Any child aged from birth to &lt;6 months with laboratory-confirmed pertussis identified from either the “Hospitalised Pertussis” study (above) or from the emergency department.</p>	<p>Despite immunisation coverage approaching 93%, pertussis continues to cause significant morbidity and mortality, particularly in very young Australian children.<sup>13</sup> The aims of this surveillance are to determine the burden of disease from hospitalised pertussis, with special emphasis on the duration of hospitalisation, use of intensive care, death and disability. Possible sources of infection and co-morbidities to severity of pertussis are examined. The adjunct study seeks to estimate the effectiveness of pertussis vaccination (either in infancy or maternal) against pertussis hospitalisations and emergency department presentations by comparing pertussis vaccination status in infants with pertussis &lt;6months of age and test-negative controls. These surveillance data will assist in optimising pertussis prevention strategies.</p>
<p><b>Varicella–Zoster Virus (VZV) Infection</b>  <i>Case definition:</i>                      Any child aged birth to &lt;15 years hospitalised for varicella or herpes zoster with or without complications.</p>	<p>Complications of varicella or herpes zoster requiring hospitalisation provide a measure of disease burden and severity. Ongoing surveillance aims to show trends in incidence and severity of both varicella and herpes zoster related to the varicella vaccination program and allow vaccine effectiveness estimations.<sup>14</sup> The timely collection of vesicle samples and genetic subtyping of varicella-zoster virus infection allows for identification of vaccine failures in immunised children and genotypes associated with severe complications or derived from the live attenuated vaccine.</p>

Condition and case definition	Rationale
<b>Invasive Meningococcal Disease (IMD)</b> Any child aged birth to <18 years who is hospitalised with laboratory confirmed invasive meningococcal disease.	Invasive Meningococcal Disease (IMD) causes death in young healthy children and adolescents in 5-10% of cases. <sup>15-17</sup> No other infectious disease has such debilitating consequences following resolution of the infection, with 20-57% of surviving children developing long term complications including amputation, cerebral infarction and severe skin scarring. <sup>18-20</sup> Surveillance of IMD will enable identification of serogroup/genotypes causes and any associations between severity of disease and sequelae. This study also seeks to estimate vaccine effectiveness against Men B infection and disease severity in IMD cases pre and post introduction of Men B vaccine in Australia.
<b>Invasive Group A Streptococcus (IGAS)</b> Any Child aged birth to <18 years hospitalised with laboratory confirmed invasive group A streptococcus disease.	The group A beta-haemolytic streptococcus is a common infective agent in children and adults that causes the widest range of clinical disease in humans of any bacterium. Invasive disease (IGAS identified in a sterile site) is less common, but has high rates of mortality and long-term morbidity. Group A streptococcal toxin mediated diseases include streptococcal toxic shock syndrome (STSS), which is usually found in association with invasive disease and has a case fatality rate over 50%. <sup>21,22</sup> There is no vaccine currently available for prevention of streptococcal infection although research is underway. Further epidemiological data on incidence, severity, clinical features and pathogen characteristics (genotype) are warranted.

\*SANE – Serious acute neurological event

## Results

In 2016, there were 174,840 admissions at the 6 participating PAEDS sites (Table 2). There were 673 cases identified across all PAEDS conditions under surveillance and sites in 2016 (Table 3). Data on an additional 227 control cases (influenza test-negative ARI cases) were collected

under FluCAN surveillance. Since PAEDS inception in 2007 a total of 5,570 cases (excluding controls) have been recruited.

### Surveillance results for 2016

Table 3 shows case numbers for all 8 conditions in 2016 and details of auditing and ICD-coded hospital discharge data.

**Table 2: Total hospital admissions and ED presentations (inclusive of admitted patients) for the 6 hospitals participating in PAEDS in 2016**

PAEDS site	Hospital admissions	ED presentations	Total PAEDS cases all conditions (% hospital admissions)*
CHW, Sydney <sup>‡</sup>	32,834	57,379	245 (1.0)
RCH, Melbourne	47,624	87,806	85 (0.2)
WCH, Adelaide	21,921	46,175	42 (0.2)
PMH, Perth <sup>‡</sup>	27,571	62,474	192 (1.0)
LCCH, Brisbane	39,945	65,713	105 (0.3)
RDH, Darwin <sup>†</sup>	4,945	14,440	4 (0.02)
<b>Total</b>	<b>174,840</b>	<b>333,987</b>	<b>673 (0.4)</b>

\*Denominator used is hospitalisations. Some cases of intussusception, pertussis (< 6months of age for VE study) or AFP (though rarely), may not be included as they may be treated in ED only.

<sup>†</sup>RDH case numbers pertain to recruitments from the second half of 2016 only, total hospital admission and ED numbers represent the full calendar year.

<sup>‡</sup>CHW (Sydney) and PMH (Perth) attained higher case numbers as they were the only PAEDS hospitals involved in influenza surveillance in 2016.

**Table 3: Number of cases captured by PAEDS in 2016 by condition and method of case ascertainment**

Condition	Case identification methods			Total captured cases (surveillance and ICD-10 audit combined)
	Total cases captured by active surveillance	Number captured by PAEDS only, not ICD-coded*	Number captured retrospectively following ICD-10 audit	
Acute flaccid paralysis <sup>†</sup>	51	29	2	53
Acute childhood encephalitis	156	72	6	162
Influenza <sup>‡</sup>	229	–	–	229
Intussusception	50	6	2	52
Pertussis <sup>§</sup>	58	7	2	60
Varicella or Herpes Zoster	57	9	5	62
Invasive Meningococcal Disease <sup>  </sup>	7	0	7	14
Invasive Group A Streptococcus <sup>  </sup>	23	3	18	41
<b>Total</b>	<b>631</b>	<b>126</b>	<b>42</b>	<b>673</b>

\*These cases did not have an ICD-10 code for this hospitalisation that was consistent with the condition diagnosed.

<sup>†</sup> AFP numbers may differ from those published in APSU and/or VIDRL reports due to differences in surveillance systems.

<sup>‡</sup> Influenza – an additional 227 control cases were captured at CHW (Sydney) and PMH (Perth). No ICD audit was carried out on this condition.

<sup>§</sup> Pertussis VE study commenced 1 July 2016 - an additional 29 control cases were captured across all sites.

<sup>||</sup> Invasive Meningococcal and Invasive Group A Streptococcus diseases commenced 1 July 2016 with a large proportion from retrospective recruitment via ICD audit due to staggered commencement from participating PAEDS sites.

### Acute flaccid paralysis

PAEDS reported 53 cases of AFP to the NERL in 2016, meeting the surveillance target of one non-polio AFP case per 100,000 children aged <15 years<sup>4</sup> (estimated Australian population in this age group is 4.58 million).<sup>23</sup> Of the 53 cases, at least one stool sample was collected within 2 weeks of onset of paralysis for 38 cases (72%), and 2 stool samples were collected for 28 cases (53%). The most common diagnoses associated with AFP were Guillain-Barré syndrome (GBS; 26%), transverse myelitis (26%) and acute demyelinating encephalomyelitis (ADEM; 15%).

### Acute childhood encephalitis

PAEDS identified 162 cases of suspected ACE in 2016. Amongst these cases were 89 (55%) with confirmed encephalitis. Amongst these were 46 (52%) with infectious causes, 32 (36%) with immune-mediated causes and 11 (12%) with

unknown causes. The leading infectious causes were human parechovirus, influenza, enteroviruses, *Mycoplasma pneumoniae*, and bacterial meningo-encephalitis.

### Serious acute neurological events (SANE) following influenza immunisation

Vaccine data from AFP and ACE surveillance was reviewed in combination. During 2016, 43 SANE in children aged <5 years were identified (23 confirmed and 7 probable encephalitis, 3 GBS, 2 ADEM, one acute cerebellar ataxia; and 4 undiagnosed acute flaccid paralysis). Only one of the 43 children had received an influenza vaccine; and this child had been vaccinated within 42 days of symptom onset. She presented to hospital with progressive proximal weakness in her lower legs and an inability to walk 7 days following receipt of influenza vaccine. She was diagnosed with transverse myelitis and had adenovirus detected in a stool specimen.

SANE cases were reported via AusVaxSafety influenza monthly and annual reports to the Commonwealth Department of Health.

## Influenza

There were 229 children with laboratory-confirmed influenza admitted to CHW (n=124) and PMH (n=105) in the 2016 season (April – October). Of these, 201 children were aged  $\geq 6$  months and 28 were aged  $< 6$  months. In addition, 227 influenza test-negative controls were enrolled in order to calculate vaccine effectiveness. Of all influenza confirmed cases, 16 (7%) were admitted to the intensive care unit, and 106 (46%) had underlying medical conditions. In children aged  $\geq 6$  months, influenza vaccination status was ascertained in 192 cases with 17 (9%) vaccinated. Of 166 controls, 23 (14%) were reported to be vaccinated. In infants under 6 months maternal vaccination status was ascertained in 19 paired mothers with 3 (16%) being vaccinated for influenza. There were 63 controls aged  $< 6$  months and maternal vaccination status was ascertained in 40 mothers. Of these, 9 (23%) were vaccinated during their pregnancy.

## Intussusception

Of the 52 cases of IS identified, 37 (71%) met level 1 Brighton Criteria.<sup>9</sup> Nine cases (24%) had received a rotavirus vaccine in the preceding 21 days: one after their first dose of vaccine, 3 after their second dose, and 5 after their third dose. Three (33%) of the 9 children required surgery to correct the IS and 6 (67%) children were successfully treated with air enema. Among all 37 cases of level 1 IS, 12 (32%) children required surgery and 25 (68%) resolved following air enema.

## Pertussis

There were 57 children hospitalised with laboratory-confirmed pertussis in 2016. Thirteen children (23%) required admission to the intensive care unit; 23% (n=13) were  $< 3$  months of age. For the adjunct vaccine effectiveness study, 8 infants aged less than 6 months were enrolled,

this included an additional 3 cases identified from the emergency department. For this study component, 29 controls were also enrolled.

## Varicella and Herpes Zoster

In 2016, 62 cases of varicella-zoster virus infection were identified (40 varicella; 22 herpes zoster). Of these, vesicular fluid or vesicle scraping samples were obtained from 27 (44%); in many children sampling was difficult as vesicles had crusted over by the time the child was identified. Of the 62 children, 43 (69%) were eligible for NIP-funded varicella vaccination but only 26 (60%) had been vaccinated.

## Invasive Meningococcal Disease

From July 2016, 14 cases of IMD were identified across the PAEDS network. Nine (64%) cases were aged less than 5, of which 3 were  $< 12$  months of age. Four (29%) cases were aged between 5 and 10, and 1 (7%) was aged  $> 10$ . Of all cases, serogroup B was the predominating strain with 9 cases overall, 7 (78%) of these were in children aged less than 5. Serogroup W was identified in 4 cases; for one case serogroup/genotype was not able to be determined. All children were of eligible age for vaccination, with 10 (71%) vaccinated for meningococcal C. No children were vaccinated for meningococcal B. Seven cases (50%) exhibited meningitis on presentation and 8 (57%) were septicaemic. Two of these children had both meningitis and septicaemia. The most common reported symptoms on presentation were fever 13 (93%), lethargy 13 (93%), rash 12 (86%) and vomiting 11 (79%).

## Invasive Group A Streptococcus

For the period 1 July to 31 December 2016, there were 45 children hospitalised with laboratory confirmed Invasive Group A streptococcus identified across all PAEDS sites. Thirty-one (69%) cases were male, and 31 (69%) were under the age of 5-years. Nineteen children (42%) were admitted to ICU, 14 within the first 24hrs of presentation to hospital. Eight children (18%) were classed as severe disease (intubated with

mechanical ventilation or inotropic support) and 2 (4%) classed as very severe disease (extracorporeal membrane oxygenation (ECMO)). The average duration of antibiotics (both IV and oral) was 26 days (range 1-79 days). The mean number of days spent in ICU was 4 days (range 1-13), with a mean of 9 days (range 1-27) spent on the ward.

## Discussion

PAEDS provides novel and unique data on hospitalisations due to uncommon serious childhood conditions, particularly VPDs and potential AEFI. Active case finding by specialist surveillance nurses and collection of detailed clinical and laboratory information provides comprehensive and timely data not available from other surveillance systems. The waiver of consent framework for surveillance allows vitally important information to be captured from otherwise hard-to-reach groups, such as those who are critically ill, lost to follow-up, or from a non-English speaking background (NESB), thereby obtaining more complete data from the broader population. Quality assurance processes such as ICD-10-AM audits, periodic case reviews and continued data management have enhanced both the yield and quality of the data captured.

PAEDS surveillance for AFP continues to provide the majority of cases for national surveillance, enabling Australia to meet the WHO AFP surveillance target<sup>4</sup> for 2016. Achieving the WHO stool collection target of 2 stool samples within 2 weeks remains challenging in the context of a modern health system where a non-polio AFP diagnosis is rapidly available<sup>24</sup>; however, PAEDS nurses facilitated collection of at least one stool sample in 71% of PAEDS AFP cases ascertained in 2016.

PAEDS encephalitis surveillance is realising its potential to support early detection of epidemic infectious diseases in children. In addition, arising out of the surveillance is the largest cohort of all-cause childhood encephalitis cases in the world that will be used to define the contempo-

rary causes and consequences of this challenging condition. Preliminary data from this cohort has been presented at the Infectious Diseases Society of America ID Week in 2016<sup>25</sup> and the European Congress of Clinical Microbiology and Infectious Diseases in 2017.<sup>26</sup> In a combined analysis of PAEDS-ACE surveillance data and PAEDS-FluCAN surveillance data, the contribution of seasonal influenza to neurological disease in children in Australia was estimated and the clinical features and outcome of influenza associated encephalopathy/encephalitis described.<sup>27,28</sup> PAEDS-ACE investigators are currently seeking to continue ACE surveillance, but reduce the burden of detailed data collection for research, and improve efficiency of case review and reporting.

Surveillance of serious acute neurological events following influenza vaccination offers confidence in the influenza vaccines of 2016, with only one noted to be proximate to an acute flaccid paralysis episode (diagnosis: transverse myelitis). Due to low number of cases ascertained an association cannot be determined. However, developing this novel methodology to monitor for severe and infrequent vaccine adverse events supports Australia's existing suite of influenza vaccine safety monitoring, and could be expanded to other vaccine types such as pertussis booster vaccination, human papillomavirus vaccine etc.

PAEDS contributes important paediatric data to national influenza surveillance in collaboration with FluCAN.<sup>29</sup> Influenza vaccines are adjusted each year to provide optimal coverage against circulating influenza strains, so ongoing surveillance is critical to understanding disease burden, vaccine efficacy and evaluate vaccination program strategies. In 2016, a quadrivalent influenza vaccine was made available under the National Immunisation Program following a higher than usual presence of influenza B in 2015.<sup>30,31</sup> Despite this, data collected from PAEDS showed that vaccine uptake in children  $\geq 6$  months was extremely low at 11% (across cases and controls) and similarly for infants  $< 6$  months; where maternal vaccination could be ascertained, uptake was only 20%. In 2016,

influenza A was the predominating strain in circulation and the available vaccine was considered to have been a good match. Estimates of vaccine effectiveness from FluCAN used PAEDS data and additional paediatric data from other hospitals, providing a point estimate of 36% (95% CI: -27%, 68%) in children aged 6 months and older, and a maternal vaccination effectiveness assessment of 44% (95% CI:-50%, 66%) for infants < 6 months.<sup>32</sup> PAEDS FluCAN surveillance for 2016 was restricted to 2 sites (WA and NSW). As of 2017, an additional 4 sites have now engaged in active influenza surveillance. These data obtained now nationally from the PAEDS network on paediatric influenza requiring hospitalisation are important to inform future policy and practice.

PAEDS data has been instrumental in quantifying the association between IS and rotavirus vaccine when given to infants.<sup>11,12,33</sup> Given the documented but low vaccine-associated risk, IS surveillance continues. Analysis of the >500 IS cases for which PAEDS holds detailed clinical data is underway to compare the clinical characteristics of vaccine proximate cases with non-vaccine proximate cases.

Pertussis continues to be one of the least well controlled VPDs in Australia.<sup>34</sup> Infants too young for vaccination, or those for whom vaccination is delayed, are at the highest risk of severe morbidity and mortality.<sup>13,35</sup> Since 2015, early infant protection via maternal vaccination during each pregnancy has been recommended.<sup>35-37</sup> The expansion of the pertussis surveillance in 2016, through an NHMRC partnership grant (ID1113851) to collect controls and undertake maternal vaccine effectiveness analysis will provide an important contribution in understanding the role of this strategy in the Australian context.

PAEDS VZV data from 2016, shows an increase in case numbers from previous years<sup>1,2</sup> and the proportion of children vaccinated was 60%. This is similar to 2015 (64%)<sup>1</sup>, though decreased from earlier years (2007-2014 78%)<sup>2</sup>. Analysis of 2007-2015 data with controls has estimated VE

for one dose of vaccine against hospitalised varicella to be 64.6% (95% CI: 46.1–76.7%); adjusting for immunocompromised children and time since vaccination did not significantly alter VE estimates.<sup>38</sup> Despite a moderate VE, Australia's program has impacted on varicella and zoster virus disease burden. Continued surveillance through the PAEDS network provides the only nationally consistent, verified source of data for severe varicella and herpes zoster, enabling ongoing evaluation of varicella vaccination under the NIP.

Clinical features of meningococcal disease are not captured in adequate detail in current IMD surveillance programs. PAEDS offers the ability to monitor changes in clinical presentation and sequelae which may relate to changes in the epidemiology of disease such as with the recent increase in serogroup W disease in Australia. As many states have now introduced meningococcal ACWY vaccine programs, monitoring the impact of these programs including severity of disease and any vaccine failures is an important priority.

The results obtained for IGAS across the PAEDS network over 6 months are similar to that found in the 2-year pilot data at RCH Melbourne (28 cases).<sup>39</sup> Due to our strict inclusion of cases from sterile sites only, a number of seriously ill children who had Group A Streptococcus isolated from 'non-sterile' sites such as abscesses or deep wounds had to be excluded. This may need to be revised in future surveillance to ensure all severe cases are able to be captured. There is increasing awareness about this important invasive infection. IGAS is currently only notifiable in Queensland and the Northern Territory and ongoing data collection is imperative in providing an evidence base to support its recognition as a potentially national notifiable disease. The in-depth clinical data we collect will also be particularly important in supporting the potential introduction of a vaccine for group A streptococcus disease in the near future.

From 2016, PAEDS activities have expanded to incorporate social research which is also

supported through the NHMRC partnership grant. This component seeks to use captured cases and conduct detailed research into the knowledge and attitudes of families of children hospitalised with influenza and pertussis, with the aim of developing improved strategies to better protect young infants. Following ethics approval attained late 2016, recruitment is set to commence in 2017.

In 2016, PAEDS was operational across 6 tertiary paediatric hospitals based in large metro-

politan centres, limiting surveillance coverage to populations served by these hospitals. In 2017, a seventh hospital: Monash children's Hospital will join the network and engage in surveillance activities for a number of PAEDS conditions.

PAEDS continues to be an important capacity-building initiative to enhance existing public health surveillance for serious childhood conditions, particularly VPDs and AEFIs, with the overarching aim of improving child health outcomes. This unique surveillance platform

**Table 4. Table of Acronyms**

<b>Acronym</b>	<b>Definition</b>
<b>ACE</b>	Acute Childhood Encephalitis
<b>ACIR</b>	Australian Childhood Immunisation Register
<b>ADEM</b>	Acute Demyelinating Encephalomyelitis
<b>AEFI</b>	Adverse events following immunisation
<b>AFP</b>	Acute Flaccid Paralysis
<b>APSU</b>	Australian Paediatric Surveillance Unit
<b>ARI</b>	Acute Respiratory Illness
<b>CHW</b>	The Children's Hospital at Westmead
<b>ED</b>	Emergency department
<b>FluCAN</b>	Influenza Complications Alert Network
<b>FS</b>	Febrile Seizures
<b>GBS</b>	Guillain Barre Syndrome
<b>ICD</b>	International Classification of Diseases
<b>IMD</b>	Invasive Meningococcal Disease
<b>IGAS</b>	Invasive Group A Streptococcus
<b>IS</b>	Intussusception
<b>LCCH</b>	Lady Cilento Children's Hospital Brisbane
<b>NCIRS</b>	National Centre for Immunisation Research and Surveillance
<b>NERL</b>	National Enterovirus Reference Laboratory
<b>NESB</b>	Non-English Speaking Background
<b>NHMRC</b>	National Health and Medical Research Council
<b>NIP</b>	National Immunisation Program
<b>NSW</b>	New South Wales
<b>PAEDS</b>	Paediatric Active Enhanced Disease Surveillance
<b>PMH</b>	Princess Margaret Hospital Perth
<b>RCH</b>	The Royal Children's Hospital Melbourne
<b>SANE</b>	Serious Acute Neurological Event
<b>VE</b>	Vaccine Effectiveness
<b>VIDRL</b>	Victorian Infectious Diseases Reference Laboratory
<b>VPD</b>	Vaccine Preventable diseases
<b>VZV</b>	Varicella Zoster Virus
<b>WCH</b>	The Women's and Children's Hospital Adelaide
<b>WHO</b>	World Health Organisation

also has the potential to be used for other urgent or research-focused studies for which active surveillance is optimal. More information on PAEDS is available at [www.paeds.edu.au](http://www.paeds.edu.au).

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