

# PAEDIATRIC ACTIVE ENHANCED DISEASE SURVEILLANCE INAUGURAL ANNUAL REPORT, 2014

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## Abstract

**Introduction:** The Paediatric Active Enhanced Disease Surveillance (PAEDS) network is a hospital-based active surveillance system employing prospective case ascertainment of selected uncommon vaccine preventable diseases and potential adverse events following immunisation (AEFI). PAEDS enhances other Australian surveillance systems by providing prospective detailed clinical and laboratory data for the same child.

**Methods:** Specialist surveillance nurses screen hospital admissions, emergency department records, laboratory and other data, to prospectively identify hospitalised children aged under 15 years in 5 paediatric tertiary referral hospitals in New South Wales, Victoria, South Australia, Western Australia and Queensland. Standardised protocols and case definitions are used across all sites. Conditions under surveillance include vaccine preventable diseases: acute flaccid paralysis, varicella, pandemic and seasonal influenza and pertussis, and potential AEFIs: febrile seizures and intussusception. PAEDS also conducts surveillance for acute childhood encephalitis.

**Results:** Since August 2007, PAEDS has recruited a total of 6,227 hospitalised cases in total, for all conditions. From January to December 2014, there were 1,220 cases recruited across all conditions. Key outcomes include: enhanced acute flaccid paralysis surveillance to reach World Health Organization targets; supporting varicella and influenza vaccination in children; confirmation of a known low risk of febrile seizures following the 1st dose of measles-mumps-rubella vaccine but no increased risk of febrile seizures after measles-mumps-rubella-varicella vaccine, and a slightly increased risk of developing intussusception 1–7 days after rotavirus vaccination in infants aged less than 3 months. Acute childhood encephalitis data facilitated rapid investigation and response to the enterovirus 71 outbreak in 2013–2014.

**Conclusions:** PAEDS provides unique policy-relevant data. This is the first of planned PAEDS annual reports to *Communicable Diseases Intelligence*. *Commun Dis Intell* 2016;40(3):E391–E400.

**Keywords:** hospital-based; surveillance; immunisation

## Introduction

In 2007, the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases, the Australian Paediatric Surveillance Unit (APSU) and a network of experts in immunisation and infectious diseases joined forces to develop a hospital-based active surveillance system: Paediatric Active Enhanced Disease Surveillance (PAEDS).<sup>1</sup> PAEDS provides important data on vaccine preventable diseases (VPDs) and adverse events following immunisation (AEFI), which are sufficiently severe to result in hospitalisation or emergency department presentation for select conditions, and difficult to adequately capture through passive surveillance mechanisms. PAEDS enables timely, prospective case identification and ascertainment, collection of detailed clinical data, medical and vaccination history, and biological samples from the same child.<sup>1</sup> For conditions where longer term outcomes are relevant, patients may be followed up after discharge from hospital.

Initially, 4 hospitals participated: The Children's Hospital at Westmead, Sydney, New South Wales; the Royal Children's Hospital, Melbourne, Victoria; the Women's and Children's Hospital, Adelaide, South Australia; and the Princess Margaret Hospital, Perth, Western Australia. In 2013, the Royal Children's Hospital, Brisbane, Queensland, joined PAEDS; this hospital moved and amalgamated in 2014 and is now the Lady Cilento Children's Hospital. Each of the 5 participating states' health departments now also contribute funding to support activities and PAEDS currently produces monthly data reports for all funding bodies and collaborators. The 5 paediatric hospitals have an estimated 148,920 admissions per annum (Table 1), representing approximately 72% of all admissions (~204,431) to tertiary hospitals providing specialist paediatric services in Australia.<sup>2</sup>

PAEDS is a separate surveillance mechanism from the APSU which relies on passive reporting from paediatricians.

In August 2007, PAEDS began surveillance of 4 conditions, including 2 VPDs and 2 AEFIs of public health and clinical interest: acute flaccid paralysis (AFP), hospitalised varicella, intussusception (IS) and seizures in infants (Table 2). PAEDS

also conducted active prospective surveillance for febrile seizures (FS) following measles-containing vaccines from 2013 to 2014, under funding by the Australian Government Department of Health as part of the vaccine safety plan for the introduction of measles-mumps-rubella-varicella (MMRV) vaccine to the National Immunisation Program (NIP). MMRV vaccine was associated with an increased risk of FS when used as the 1st dose of a measles-containing vaccine in the United States of America.<sup>3</sup> A retrospective review of FS (from January 2012 to April 2013) to investigate the risk of FS post-MMR (dose 1) and varicella vaccine was also conducted.<sup>4</sup>

PAEDS also conducted surveillance for children aged under 15 years with laboratory proven influenza during the influenza pandemic who were hospitalised during the period June to October 2009. This was funded by a National Health and Medical Research Council grant (no.633028) and supplemented by additional funding from the NSW Ministry of Health, enabling recruitment of influenza cases at 2 additional hospitals in New South Wales: John Hunter Children's Hospital, Newcastle and the Sydney Children's Hospital, Randwick.<sup>7</sup> The protocol and data collection forms were developed quickly by adapting the existing APSU protocol.<sup>9</sup>

**Table 1: Total hospital admissions and emergency department presentations for the 5 hospitals participating in Paediatric Active Enhanced Disease Surveillance in 2014**

Hospital	Hospital admissions	Emergency department presentations
Children's Hospital at Westmead, Sydney	32,149	55,049
Royal Children's Hospital, Melbourne	45,548	83,970
Women's and Children's Hospital, Adelaide	21,101	46,289
Princess Margaret Hospital, Perth	28,910	70,834
Lady Cilento Children's Hospital, Brisbane	21,212	26,773
Total	148,920	282,915

**Table 2: Paediatric Active Enhanced Disease Surveillance conditions under surveillance, case definitions and rationale, 2007–2014**

Condition and case definition	Rationale
<p>Acute flaccid paralysis (AFP) (2007 – ongoing)</p> <p><i>Case definition:</i></p> <p>Any child aged up to 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>The World Health Organization requires active national surveillance for cases of AFP in children aged &lt;15 years in order to monitor for potential cases of paralytic poliomyelitis. Because of long-standing problems in obtaining adequate reporting and stool collection rates (at least 1/100,000 AFP cases in children &lt;15 years of age and collection of 2 stool specimens within 14 days of onset of paralysis in all identified cases), AFP was considered as a priority condition for inclusion in Paediatric Active Enhanced Disease Surveillance (PAEDS). PAEDS collects ~77% of all AFP cases identified annually in Australia.</p>
<p>Intussusception (2007 – ongoing)</p> <p><i>Case definition:</i></p> <p>Any child aged &lt;24 months presenting with a diagnosis of acute intussusception confirmed on air/liquid contrast enema or surgery (i.e. based on Level 1 of Diagnostic Certainty using the Brighton Collaboration clinical case definition). Includes hospitalised or emergency department only.<sup>5</sup></p> <p>From May 2013 the case definition age changed to &lt;9 months.</p>	<p>Intussusception is the most common cause of bowel obstruction in infants and young children and was associated with a previous rotavirus vaccine withdrawn from the United States of America in 1999. Timely, active and systematic surveillance of intussusception cases has been important to identify any temporal association with the 'new generation' rotavirus vaccines funded under the National Immunisation Program (NIP) from July 2007. Surveillance also aims to describe the epidemiology, aetiology and severity of intussusception.</p>
<p>Varicella and zoster hospitalisations (2007 – ongoing)</p> <p><i>Case definition:</i></p> <p>Any child aged 1 month to &lt;15 years hospitalised for varicella-zoster virus infection with or without complications.</p>	<p>Varicella vaccination was funded under the NIP from late 2005. Complications of varicella requiring hospitalisation provide a measure of disease burden and severity. Ongoing surveillance may show trends in both varicella and herpes zoster related to the varicella vaccination program and allow vaccine effectiveness estimations. The timely collection of vesicle samples and genetic subtyping of varicella-zoster virus allows for identification of vaccine failures in immunised children and genotypes associated with severe complications.</p>

**Table 2 continued: Paediatric Active Enhanced Disease Surveillance conditions under surveillance, case definitions and rationale, 2007–2014**

Condition and case definition	Rationale
<p>Seizures (August 2007–2008)</p> <p><i>Case definition:</i></p> <p>Any child aged 1 to &lt;8 months who presents with seizures and meets the following criteria: first seizure presentation AND there is no identifying trauma (e.g. head injury) AND the hospital stay is 4 hours or more.</p>	<p>Infants presenting with seizures in the first 8 months of life are of interest because seizures are a recognised potential serious adverse event following vaccination. Surveillance for infantile seizures provides an opportunity to describe the temporal relationship between seizures and recent vaccination.</p> <p>This surveillance was discontinued in 2008, in part due to the difficulty of applying the case definition in young infants, in whom the presentation of seizures can be complex to diagnose.</p>
<p>Febrile seizures following measles-containing vaccines (May 2013 – June 2014)</p> <p><i>Case definition:</i></p> <p>Any child aged &lt;5 years who presents with a seizure that fulfils the Brighton Collaboration case definition for a seizure AND occurs within 48 hours of an inactivated vaccine and/or 14 days of a live attenuated vaccine AND is associated with fever documented either by a parent and/or health provider.</p>	<p>Use of measles-mumps-rubella-varicella (MMRV) combination vaccine as the first dose of measles-containing vaccine in the United States of America was found to double the risk of fever and febrile seizures in children aged 12–23 months in the 5–12 days after vaccination (when compared with children who received MMR and varicella vaccines as separate injections).<sup>3</sup> In July 2013, MMRV vaccine was included on the NIP as the 2nd dose of measles-containing vaccine. Surveillance (retrospective and prospective) for febrile seizures following MMR, varicella and then MMRV vaccine was conducted to determine the risk of febrile seizures occurring after each vaccine as used under the Australian NIP.</p>
<p>Pertussis (2012 – ongoing)</p> <p><i>Case definition:</i></p> <p>Any child aged birth to 15 years (ineligible as of 15th birthday) admitted to hospital with laboratory-confirmed pertussis.</p>	<p>Despite immunisation coverage approaching 90% (for the 3 primary doses of diphtheria-tetanus-pertussis vaccine in pre-school children), pertussis continues to cause significant morbidity and mortality in Australian children.<sup>6</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. The contribution of comorbidities to the severity of pertussis and possible sources of infection will also be examined. This surveillance data will assist in optimising pertussis prevention strategies.</p>
<p>Influenza – pandemic (June–October 2009)</p> <p><i>Case definition:</i></p> <p>Any child aged &lt;15 years at the time of diagnosis of influenza confirmed by laboratory testing, and admitted to hospital.</p>	<p>Children may suffer severe complications from influenza, including encephalopathy, myocarditis and rhabdomyolysis. Timely detailed data describing pre-existing risk factors, presentation, clinical course and outcome in children hospitalised with influenza, including H1N1-09, were lacking. Such data were needed to inform vaccination policy and clinical practice, as well as to assess the effectiveness of outbreak response measures.</p>
<p>Influenza – FluCAN (April–October each year. Commenced 2014)</p> <p><i>Case definition:</i></p> <p>Any hospitalised child aged &lt;18 years who presents with suspected influenza (respiratory symptoms +/- fever) who is positive for influenza by polymerase chain reaction.</p>	<p>The emergence of H1N1-09 influenza in 2009 demonstrated the importance of enhanced surveillance in children.<sup>7</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 influenza surveillance data collected by the other 15 sites under the FluCAN network. Information on influenza test negative (control) patients with acute respiratory illness is also collected and allows calculation of vaccine effectiveness to be performed.</p>
<p>Acute childhood encephalitis (2013 – ongoing)</p> <p><i>Case definition:</i></p> <p>Any child aged &lt;15 years AND hospitalised with acute encephalopathy AND 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 requires hospitalisation and is considered a marker syndrome for emerging infectious diseases. It is most often caused by viruses (including those that are or potentially will be vaccine preventable). It can also be immune-mediated, and uncommonly can be associated with vaccine receipt. Although a potentially preventable cause of mortality and morbidity in children, there are limited epidemiologic data on encephalitis. PAEDS is uniquely placed to undertake active, syndromic surveillance with the additional capacity to collect biological specimens and enrol participants into comprehensive follow-up studies to improve understanding of long-term neuropsychological sequelae.<sup>8</sup></p>

From 2014, active prospective surveillance for influenza has been resumed at 2 PAEDS sites (Sydney and Perth) in collaboration with the Influenza Complications Alert Network (FluCAN) surveillance system, established in multiple adult and general hospitals.<sup>10,11</sup> Surveillance for acute childhood encephalitis also commenced in 2014 following a successful pilot study in New South Wales in 2013.<sup>8</sup>

In this report we summarise data collected by PAEDS between 2007 and 2014, with emphasis on the impacts and outcomes of surveillance and their potential usefulness to inform clinical practice and policy. We also provide a detailed report of surveil-

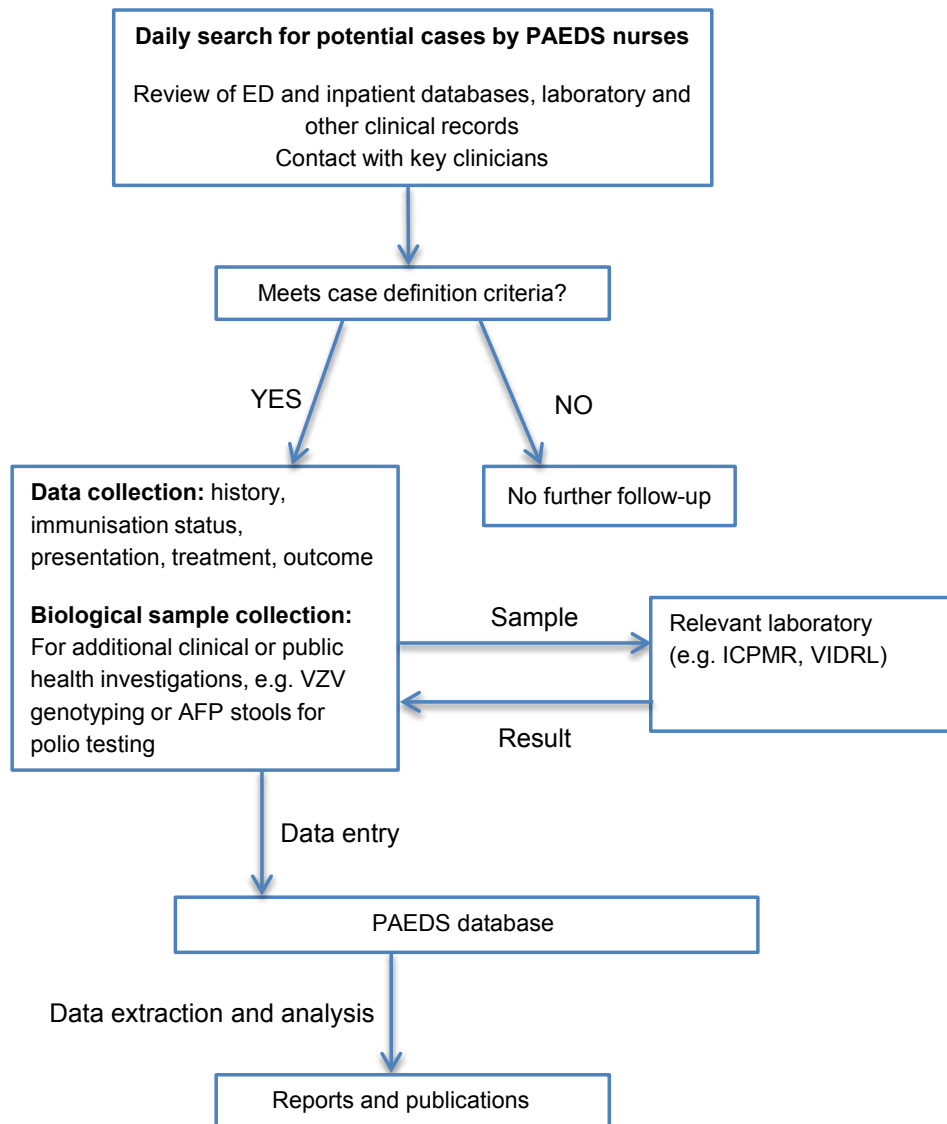
lance data for the year 2014, with a view to providing annual surveillance reports in *Communicable Diseases Intelligence* each year.

## Methods

### Active case ascertainment

Under PAEDS, specialist surveillance nurses in each hospital identified children aged less than 15 years diagnosed with the target conditions as defined in Table 2, by reviewing admission and emergency department databases and clinical records, laboratory results and/or infection control logs (Figure). Relationship-building and networking with medical and nursing staff in each hospital enhances prospective case identification.

**Figure: Overview of Paediatric Active Enhanced Disease Surveillance methods in the participating 5 sites\***



\* Participating sites are 5 sites: Children's Hospital at Westmead (Sydney), Royal Children's Hospital (Melbourne), Women's and Children's Hospital (Adelaide), Princess Margaret Hospital (Perth), Lady Cilento Children's Hospital (Brisbane)

Ethics permission was obtained from the Human Research Ethics Committees at each of the 5 hospitals. The initial model was based on consent being obtained from parents or guardians, after which detailed data were extracted from the clinical record, with data collection enhanced by interviewing the family.<sup>1</sup> In 2014, PAEDS moved to a 'no consent' model using de-identified data. By early 2015 all sites obtained ethics approval for reporting on de-identified data from clinical records, without the need to obtain written consent; families are provided with information sheets and written consent is still sought where information not collected in the medical record as part of best clinical practice is required from the family.

To check for completeness of case ascertainment, PAEDS nurses at each site conduct regular retrospective audits of medical records by searching for primary and secondary International Statistical Classification of Diseases and Related Health Problems, 10th revision, Australian Modification (ICD-10-AM) codes describing the relevant conditions (e.g. K56.1 for intussusception and BO1/BO2 and subcategories for varicella infection). Cases ascertained through the medical records audits were compared with the cases ascertained by PAEDS for the same period. Any additional cases identified by the ICD-10-AM audit process were retrospectively recruited into PAEDS.

### Collection of biological samples

Surveillance nurses facilitated collection of 2 stool samples within 14 days of onset of paralysis from children hospitalised with AFP. These samples were sent to the Australian National Enterovirus Reference Laboratory in Melbourne for identifi-

cation of enteroviruses.<sup>12</sup> Residual samples from vesicle scrapings obtained from children admitted for varicella or herpes zoster were collected and sent to the Institute for Clinical Pathology and Medical Research at Westmead Hospital in Sydney for genotyping of varicella-zoster virus. Stool samples from children with IS were analysed in local diagnostic laboratories for the presence of rotavirus (including vaccine-derived types), adenovirus and enterovirus. Residual specimens from children hospitalised with acute encephalitis were also collected and tested for unknown pathogens. Laboratory results for cases of influenza, pertussis and encephalitis were also collected and recorded in the PAEDS database.

### Data management and communication

Originally, a purpose-built Microsoft Access database was developed by APSU and deployed to participating hospitals. Since 2013, PAEDS adopted the database 'WebSpirit',<sup>13</sup> which enables online data entry by surveillance nurses at each site. Data are held securely and exported on a regular basis by staff at the PAEDS coordinating centre for clinical review, quality checks, analysis and reporting. Communication is facilitated by joint monthly teleconferences of all PAEDS investigators and nurses, as well as monthly nurse teleconferences. Detailed review of protocols and study outcomes occurs at an annual face-to-face meeting, which also facilitates planning for the introduction of new conditions into PAEDS.

### Results

From August 2007 to December 2014, PAEDS collected data on 6,227 cases of the conditions under surveillance (Table 3). Data on an additional

**Table 3: Cases ascertained through the Paediatric Active Enhanced Disease Surveillance system, August 2007 to December 2014**

Condition	Period of surveillance	Cases ascertained (n)
Acute flaccid paralysis	August 2007 – December 2014	299
Intussusception	August 2007 – December 2014	562
Varicella	August 2007 – December 2014	300
Seizures in infants aged 1–9 months	August 2007 – October 2008	126
Febrile seizures*	May 2013 – June 2014 (prospective)	1,701
	January 2012 – April 2013 (retrospective)	2,013
Pandemic influenza	June 2009 – September 2009	601 total (529 pandemic H1N1)
Pertussis	January 2012 – December 2014	201
Acute childhood encephalitis†	May 2013 – December 2014	140
Influenza (FluCAN)‡	April 2014 – October 2014	284§
Total for all conditions		6,227

\* Retrospective surveillance for febrile seizures was conducted using hospital discharge data (ICD-10-AM coding).<sup>4</sup>

† Children's Hospital at Westmead (Sydney) from 1 May 2013 and all Paediatric Active Enhanced Disease Surveillance sites progressively from 1 January 2014.

‡ Children's Hospital at Westmead (Sydney) and Princess Margaret Hospital (Perth) sites only.

§ 284 hospitalised control cases were also recruited.

284 control cases (influenza test-negative acute respiratory illness cases) were collected under FluCAN surveillance. Key results and impacts of surveillance for all conditions for 2007 to 2014 are summarised in Table 4.

### Surveillance results for 2014

Seven conditions were under surveillance during 2014, including 4 vaccine preventable diseases (AFP, varicella, pertussis and influenza [2 sites,

collaboration with FluCAN]); 2 potential AEFIs (IS and febrile seizures); and another serious disease of childhood, encephalitis. Table 5 shows case numbers for all conditions for 2014 and provides details of auditing and assessment of cases in relationship to ICD-coded hospital discharge data for select conditions. Following the move to operate under a waiver of consent framework, data on cases identified from ICD audit only have also been eligible for inclusion.

**Table 4: Key Paediatric Active Enhanced Disease Surveillance results and impacts, 2007 to 2014**

Condition	Results and impacts
Acute flaccid paralysis	<p>Cases reported to the Polio Expert Panel* for review; at least 1 stool sample collected in 72% of cases†</p> <p>The World Health Organization (WHO) surveillance target reached<sup>12</sup></p> <p>Surveillance contributes to Australia fulfilling polio-free status, as certified by the WHO</p> <p>Paediatric Active Enhanced Disease Surveillance (PAEDS) contributed cases to the WHO surveillance effort for Guillain-Barré syndrome (identified as a potential adverse event following immunisation following pandemic influenza vaccination)<sup>14</sup></p>
Varicella and zoster	<p>Number of hospitalised varicella cases has reduced since the introduction of vaccination onto the National Immunisation Program (NIP)<sup>13</sup></p> <p>Most hospitalised cases not vaccinated against varicella<sup>15</sup></p> <p>Varicella-zoster virus genotyping conducted to monitor for presence of wild and vaccine type strains<sup>15</sup></p>
Intussusception	<p>First global study demonstrating that infants aged &lt;3 months had a slightly increased risk of developing intussusception 1–7 days after the 1st dose of the new rotavirus vaccines.<sup>16</sup> Results confirmed by additional Australian and global studies.<sup>17</sup></p> <p>Informed ongoing risk–benefit analysis for vaccine program, and information for parents and providers on rotavirus vaccine safety developed</p> <p>Ongoing surveillance contributes to maintaining public confidence in rotavirus vaccines</p>
Febrile seizures	<p>Analysis showed known low risk of febrile seizures post measles-mumps-rubella dose 1, but no increased risk of febrile seizures post monovalent varicella vaccine</p> <p>Preliminary analysis to 2013–2014 shows no increased risk of febrile seizures for measles-mumps-rubella-varicella (MMRV) under the NIP (where MMRV is used as the 2nd measles-containing vaccine dose)<sup>18</sup></p> <p>Affirmed safety profile of MMRV as used under the Australian NIP</p>
Pandemic influenza (2009 only)	<p>Approximately 30% of children admitted to hospital with pandemic influenza were previously healthy, while the remainder had a chronic disorder that predisposed them to infection</p> <p>Only 17% of children who had a chronic disorder making them more vulnerable to influenza infection had been vaccinated against influenza<sup>7</sup></p> <p>Named in the National Health and Medical Research Council's 10 of the Best Projects for 2013 (grant number: 633028 under the 2009 Urgent Call for Research on H1N1 Influenza 09 to Inform Public Policy)</p>
Influenza (in collaboration with FluCAN)	<p>Inclusion of paediatric cases in FluCAN from 2014 (n=401 hospitalised cases, 284 from 2 PAEDS sites)</p> <p>Demonstrated good vaccine effectiveness against paediatric influenza hospitalisation<sup>19</sup></p> <p>Demonstrated low vaccine uptake (among control subjects) suggests need to improve influenza immunisation program</p>
Acute childhood encephalitis	<p>Pilot surveillance and protocol development helped to inform comprehensive guidelines for the investigation and management of encephalitis in Australia and New Zealand<sup>20</sup></p> <p>Facilitated rapid investigation and response to enterovirus-71 outbreak and emergence of parechovirus disease in 2013–14, incorporating cases captured by PAEDS surveillance<sup>21,22,23</sup></p>

\* The Polio Expert Panel is a subcommittee of the Communicable Diseases Network Australia. Results of acute flaccid paralysis surveillance are published annually in *Communicable Diseases Intelligence*.

† Although the World Health Organization requires 2 stool samples within 2 weeks of paralysis and at least 24 hours apart, this target is rarely reached in developing countries.<sup>24</sup>

### Influenza

In 2014, 284 paediatric cases of influenza and 284 controls were identified at the Children's Hospital at Westmead (Sydney) and Princess Margaret Hospital (Perth) sites and contributed to FluCAN surveillance. Of these 284 cases, 22 (7.8%) were admitted to the intensive care unit. There were 125 (44%) children who had chronic conditions predisposing them to influenza infection, but only 16 (6.5%) of these had received at least 1 dose of influenza vaccine in the 2014 influenza season.

### Acute flaccid paralysis

The 46 cases of AFP identified in 2014 (rate 44/100,000 children aged <15 years per annum) met the World Health Organization (WHO) AFP surveillance target. At least 1 stool sample was collected within 2 weeks of onset of paralysis for 33 cases (72%), and 2 stool samples were collected for 24 (52%) cases. The most common diagnoses associated with AFP were transverse myelitis (24%) and Guillain-Barré syndrome (39%).

### Intussusception

Of the 52 cases of IS identified in 2014, 12 (23%) had received a rotavirus vaccine in the previous 21 days. Of these 12 children, 3 had IS after the 1st dose of vaccine, 3 after the 2nd dose, and 6 after

the 3rd dose. Two of the 12 children required surgery to correct IS, 6 resolved with air enema and 4 resolved spontaneously. Among all 52 cases of IS, 7 (13.5%) children required surgery, 32 (62%) resolved with an air enema and in 13 (25.0%) cases the IS resolved spontaneously.

### Varicella

Among the 49 cases of varicella, vesicular fluid or vesicle scraping samples were obtained from 25 (51%) cases; in many children sampling was difficult as vesicles had crusted over by the time the child was admitted and approached by the PAEDS nurse. Of the 49 children, 22 (45%) were eligible for NIP-funded varicella vaccination but only 14 had been vaccinated.

### Pertussis

There were 49 children hospitalised with laboratory-confirmed pertussis in 2014. Detailed clinical data on all cases and their contacts and vaccination histories were collected. Seven children required admission to the paediatric intensive care unit. Approximately half (n=25) were under 3 months of age.

### Febrile seizures

In 2014 (January–June), 647 cases of febrile seizures were captured by PAEDS. Active surveil-

**Table 5: Cases recruited to Paediatric Active Enhanced Disease Surveillance in 2014 by condition, number and methods of case ascertainment**

Condition	Case identification methods			Total recruited cases (Surveillance and ICD-10 audit combined)
	Total cases captured via active surveillance	Number captured by PAEDS only, not ICD-coded	Number recruited retrospectively following ICD-10 audit	
Acute flaccid paralysis*	44	15	2	46
Intussusception	43	3	9	52
Varicella-zoster virus	41	8	8	49
Pertussis	45	3	4	49
Febrile seizures†	641	7	6	647
Acute childhood encephalitis‡	93	93	ND	93
Influenza§	284	284	ND	284
Total	1,191	36	29	1,220

ND = not done

\* Acute flaccid paralysis numbers may differ from that published in the Australian Paediatric Surveillance Unit and/or Australian National Enterovirus Reference Laboratory reports due to differences in surveillance systems.

† Febrile seizure surveillance period January – June 2014; Children's Hospital at Westmead (Sydney) audited only, 164 total cases of which 7 were Paediatric Active Enhanced Disease Surveillance (PAEDS) only and 6 added by audit.

‡ Acute childhood encephalitis ICD-10-AM audit incomplete at time of report.

§ Influenza – an additional 284 control cases were recruited at Children's Hospital at Westmead (Sydney) and Princess Margaret Hospital (Perth). These may include some cases separately reported to the Australian Paediatric Surveillance Unit from other sites. No ICD-10-AM audit was carried out on this condition.

lance for this condition concluded on 30 June 2014. Between 1 May 2013 and 30 June 2014, prospective surveillance identified 1,701 FS episodes in 1,471 children aged 0 to <5 years. Of these, 1,335 had only 1 FS and 136 (11%) had 2 or more episodes in the study period. Five hundred and seventy (39%) children with an FS had received MMRV vaccine at any time. PAEDS analysis of the risk of FS in various time periods up to 30 days post MMRV vaccine, using self-controlled case-series analysis, showed no vaccine-associated increase in risk.<sup>18</sup>

### *Acute childhood encephalitis*

Between May 2013 and December 2014, the surveillance identified 140 cases of suspected childhood encephalitis. An analysis of the pilot phase has shown that PAEDS performs very well in detecting cases of childhood encephalitis and has the capacity to identify cases associated with epidemic infectious diseases.<sup>21–23</sup> Approximately 3-quarters of eligible children have been recruited to follow-up studies and over half have had biological specimens salvaged for future analysis. The study is revealing key differences in the clinical features of infectious encephalitis when compared with immune-mediated encephalitis.

## Discussion

PAEDS has provided novel and unique data on hospitalisations due to selected uncommon serious childhood conditions, particularly VPDs and potential AEFI, over the last 7 years. Active case finding by specialist surveillance nurses, and collection of detailed clinical and laboratory data in the same child is unique to PAEDS.<sup>1</sup> This surveillance approach provides a rich and timely source of data that is comprehensive in nature and allows for the collection of demographic details, family history, clinical characteristics, outcome data and analysis of biological specimens, all matched to each individual patient. Such data are not available from other systems. Importantly, our detailed case ascertainment and reporting serves to enrich data collected under other systems. Comparison of PAEDS-ascertained cases with regular audits of hospital discharge data using relevant ICD-10-AM codes is conducted as part of quality assurance processes. These comparisons have shown that case ascertainment yields through PAEDS are high, and more timely than auditing medical records. PAEDS also provides additional cases not otherwise ICD-coded for the condition of interest.

PAEDS surveillance for AFP significantly enhanced surveillance conducted via the APSU and the Australian National Enterovirus Reference

Laboratory and has enabled Australia to meet the WHO AFP surveillance targets for the last 7 years.<sup>12,24</sup> 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 1 stool sample in 72% of AFP cases ascertained in 2014.<sup>25</sup>

PAEDS surveillance suggested an excess of IS cases in infants 1–7 days after receipt of the 1st dose of either of the new rotavirus vaccines currently used in Australia, the first study worldwide to describe this link.<sup>16</sup> These data informed vaccination policy and practice, stimulated additional studies and resulted in the development of educational materials for parents and vaccine providers.<sup>17</sup> Analysis of the more than 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.

The number of hospitalised cases of varicella-zoster virus has reduced with increased uptake of varicella vaccination.<sup>15</sup> Nevertheless, the majority of children (71%) hospitalised due to varicella-zoster virus infection were not vaccinated for varicella, despite being eligible under the NIP. These data support the continuation of the population-based funded varicella vaccination program in Australia, and current efforts to increase varicella vaccine coverage, such as via the inclusion of MMRV vaccine onto the NIP.

PAEDS also conducted a high intensity, short-term study of FS following measles-containing vaccines, to support the vaccine safety plan for the introduction of MMRV onto the NIP. Retrospective and prospective surveillance identified data on more than 3,700 FS presentations and, using vaccine data from the Australian Childhood Immunisation Register, we were able to analyse the risk of FS following MMR, varicella and MMRV vaccines.<sup>4</sup> The absence of an increased risk of FS following MMRV vaccine supports ongoing use of this vaccine as the 2nd dose of measles-containing vaccine at 18 months of age under the NIP.

PAEDS has the capacity to rapidly respond to disease outbreaks as shown by surveillance for influenza during the H1N1-09 pandemic,<sup>7</sup> contributions towards enterovirus 71<sup>22</sup> and parechovirus<sup>21,23</sup> outbreak investigations and, from 2014, PAEDS continues to contribute paediatric data to the influenza surveillance efforts in Australia through the collaboration with FluCAN.<sup>9</sup> PAEDS data highlights the need for improved uptake of influenza vaccination in children, particularly those who have predisposing chronic conditions.<sup>19</sup>



PAEDS reliably collects demographic details such as ethnicity, enabling potential analysis of subgroups of children with greater susceptibility to severe disease and missed opportunities for disease prevention, including missed or late immunisation. PAEDS collects laboratory data that is directly linked to clinical details and vaccination history for the same child, enabling the description of relationships between genetic subtypes and disease severity or vaccine failures. Such data are important to support development of immunisation policy and for maintaining consumer and provider confidence in the NIP. However, collection of biological samples can be challenging for a range of reasons. For example, a child might be admitted after varicella vesicles have crusted over and taking a sample of vesicle fluid is not possible, or a patient with AFP may be unable to produce a stool sample within the prescribed time period and before they are discharged from hospital.

Currently, PAEDS operates in 5 tertiary paediatric hospitals based in large metropolitan centres, limiting surveillance coverage to populations served by these hospitals. Despite this, we estimate that approximately 70% of all paediatric admissions to tertiary paediatric services are covered by PAEDS. Further expansion, especially to hospitals in northern Australia which serve Aboriginal and Torres Strait Islander populations, would enhance coverage in these vulnerable populations. Not all tertiary paediatric hospitals in New South Wales and Victoria participate in PAEDS and coverage could be significantly enhanced by including these hospitals.

PAEDS is an important capacity building initiative to enhance existing public health surveillance for VPDs and AEFIs, with the overarching aim of improving child health outcomes. This unique surveillance platform 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 on the [PAEDS web site](http://www.paeds.edu.au) (www.paeds.edu.au).

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