PAEDS Newsletter

Paediatric Active Enhanced Disease Surveillance

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the children's hospital at Westmead

The Sydney children's Hospitals Network

ncirs NATIONAL CENTRE FOR IMMUNISATION RESEARCH & SURVEILLANCE

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Welcome

Welcome to the 2016 PAEDS Newsletter. This year marks the ninth year that PAEDS has been in operation. We are proud to announce that we have been awarded a National Health and Medical Research Council (NHMRC) funded Partnership Project, and that our studies into serious childhood conditions continue apace. In this newsletter, we document the various milestones of the last year of PAEDS and look to our future horizons.

Welcoming Darwin and Monash hospitals

PAEDS is pleased to announce that the Royal Darwin Hospital, Northern Territory, is joining as one of our new surveillance sites. In addition, surveillance will be expanding in Victoria to include the new Monash Children's Hospital (planned to open in early 2017). This makes PAEDS a truly national operation, with seven surveillance sites across the country:

- The Children's Hospital at Westmead (NSW)
- Lady Cilento Children's Hospital (QLD)
- Princess Margaret Hospital for Children (WA)
- Women's and Children's Hospital (SA)
- The Royal Children's Hospital Melbourne (VIC)
- Monash Children's Hospital, Monash Medical Centre (VIC)
- Royal Darwin Hospital (NT)

PAEDS also continues to collaborate with the Australian Government Department of Health and the state and territory health departments associated with each surveillance site.

NHMRC partnership grant success

We are pleased to announce the award of an NHMRC-funded Partnership Project (ID 111430, Chief Investigator A/Prof Kristine Macartney) entitled 'Reducing vaccine preventable diseases in children: using national active hospital-based surveillance to evaluate and improve immunisation program performance'.

This project is aimed at:

- improving immunisation programs to prevent childhood illness and death due to influenza and pertussis; and
- promoting effectiveness and equity in our immunisation programs for influenza and pertussis.

Influenza and pertussis remain a significant challenge. An average of 2,700 children are hospitalised from these diseases each year. Deaths also continue to occur from these illnesses, even in previously healthy children and babies.

We will be undertaking a novel and systematic examination of how factors related to both the *effectiveness* and the *uptake* of vaccination contribute to controlling influenza and pertussis in Australian children.

The project enables us to expand upon our national PAEDS partnership in major paediatric hospitals in NSW, Western Australia, South Australia, Queensland and Victoria. We will be adding two new sites: Royal Darwin Hospital in the Northern Territory and the new Monash Children's Hospital in Victoria.

With total funding comprising 50 per cent support from the NHMRC and 50 per cent from our funding partners – the Australian Government and all relevant state and territory Departments of Health – our collaboration is well placed to conduct this cutting edge program-relevant research.

Our nationally representative team comprises immunisation and public health experts, epidemiologists and social scientists. For a full list of chief and associate investigators, please see our website: paeds.edu.au. Over the coming three years, from October 2016, we will undertake a range of studies, including:

a. identifying in whom breakthrough disease occurs despite immunisation and why, and estimating vaccine effectiveness of new programs;

b. identifying reasons for under-vaccination or no vaccination at the individual, community, system and policy levels; and

c. determining factors or gaps in immunisation policy and practice that can be changed to improve prevention of disease from influenza and pertussis in children.

10-year anniversary celebration

Next year will be the PAEDS 10-year anniversary since commencing as a pilot project in 2007. This project was commenced under the leadership of the National Centre for Immunisation Research and Surveillance (NCIRS) and the Australian Paediatric Surveillance Unit (APSU) and over the years has continued to grow across Australia. Over this time, surveillance of a number of important paediatric conditions has been included, particularly related to vaccine preventable diseases and adverse events following immunisation. We have a number of publications and have contributed to shaping policy and practice.

Keep an eye out in early 2017 for details of our 10-year anniversary celebration plans.

Update on PAEDS studies

Pertussis

All sites have been involved in active surveillance of children hospitalised with pertussis since 2012.

There have been 259 confirmed cases in total. In infants aged less than one year, there have been 183 confirmed cases and one death recorded. The introduction of newly funded vaccines, including maternal immunisation (introduced between September 2013 and June 2015 by different states and territories) and the addition of an 18-month booster vaccine in April 2016, strengthens the need to conduct high quality enhanced disease surveillance. Recent and ongoing activities also include:

- Presentation of data at the Public Health Association Australia (PHAA) National Immunisation Conference, June 2016
- Manuscript in preparation outlining clinical findings, and highlighting immunisation status of infants, mothers and household contacts
- Planned case control study to determine vaccine effectiveness in light of recent vaccine changes, under the NHMRC partnership grant.

Encephalitis

This is a landmark study of childhood encephalitis. Now in its third year of surveillance and participant recruitment, we have assembled one of the largest paediatric, all-inclusive cohorts of acute encephalitis in the world. To date, we have detected and reported two outbreaks of infectious encephalitis (from enterovirus type A71 [EVA71] and human parechovirus type 3 [HPEV3]), defined the contribution of seasonal influenza to childhood encephalitis and serious neurological disease, and established a cohort for long-term follow-up studies and biobanking of specimens. Work is ongoing to fully evaluate this large cohort to better characterise the clinical features of childhood encephalitis, especially amongst the 25 per cent of cases that have no cause identified (unknown encephalitis).

Febrile seizures

In July 2013, the combination measles-mumps-rubella-varicella (MMRV) vaccine was added to the National Immunisation Program at the scheduled age of 18 months to provide earlier two-dose protection against measles and improve varicella vaccine uptake. The PAEDS surveillance system was used to obtain prospective real-time data to inform the risk of febrile seizures (FS) with measles-containing vaccines, particularly the new MMRV vaccine.

In prospective surveillance we identified 1,668 unique FS episodes in 1,471 children aged under five years; the peak age of presentation was 18 months. In children who had previously received a dose of MMR vaccine, there was no significant increased risk of FS within the 5-12 day risk period following MMRV vaccine. A manuscript on the risk of FS after MMRV vaccine and increased vaccine coverage is in preparation.

To date, 152 children with FS have been recruited into our follow-on study led by A/Prof Nick Wood (NHMRC Project Grant 1049557) that aims to determine the risk of post-vaccination FS (PVFS) and to comprehensively categorise and describe the clinical, genetic and developmental outcomes among children who have experienced a PVFS.

Acute flaccid paralysis (AFP)

Surveillance for acute flaccid paralysis has been conducted by PAEDS since 2007 and this data has contributed to Australia fulfilling the AFP surveillance requirements of the World Health Organization (WHO) as part of the Global Polio Elimination Strategy. PAEDS collects over 75 per cent of all AFP cases identified annually in Australia with 46 cases recruited nationally by PAEDS in 2015.

Severe acute neurological events (SANE)

During 2015 and 2016, PAEDS captured and assessed vaccine exposure in children admitted with severe acute neurological events (SANE), such as encephalitis, Guillain-Barré syndrome (GBS) and transverse myelitis. Vaccine history data is verified and medical records are examined to assess any potential temporal relationship to vaccine administration, particularly for influenza vaccine. As case numbers accumulate, we hope to be able to use analytical methods to confirm our hypothesis that severe neurological adverse events are not associated with receipt of vaccines. This surveillance can also help provide reassurance to the public regarding vaccine safety, in conjunction with other systems for active prospective surveillance, such as that done under the AusVaxSafety network (ncirs.edu.au/surveillance/ausvaxsafety/index.php).

Intussusception

Surveillance for intussusception (a rare form of bowel blockage) commenced in 2007 in all PAEDS sites. PAEDS data has demonstrated a small but significant risk of intussusception among young infants in the weeks following the first two doses of rotavirus vaccine. In 2015, 65 infants with intussusception were identified and recruited by the PAEDS network. Further analysis is now being undertaken looking at clinical severity and outcomes of intussusception.

Influenza

From 2014, PAEDS, in collaboration with the Influenza Complications Alert Network (FluCAN), resumed surveillance of influenza. PAEDS provides unique timely sentinel data from two sites (Sydney and Perth) on influenza hospitalisations, including complications and deaths. 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 is also collected and allows vaccine effectiveness to be calculated and reported to WHO. Analysis has demonstrated very low vaccine uptake (among control subjects) which suggests a need to improve paediatric influenza immunisation in Australia. Good vaccine effectiveness against influenza hospitalisation in children has been reported. Influenza surveillance will expand across the whole PAEDS network in the coming 12 months, under the NHMRC partnership grant.

Varicella-zoster

All PAEDS sites have been involved in active surveillance of children hospitalised with varicella-zoster virus since 2007. There have been 336 cases in total. Recent and ongoing activities also include:

- Presentations of data at the PHAA National Immunisation Conference, June 2016
- Manuscript to be submitted shortly describing the effectiveness of a single dose of varicella vaccine against hospitalised varicella
- Manuscript in preparation outlining clinical features of severe and complicated varicella and any association with genotypes.

Update on new conditions

Invasive meningococcal disease (IMD)

Invasive meningococcal disease (IMD) causes death in young healthy children and adolescents in 5-10 per cent of cases. No other infectious disease has such debilitating consequences following resolution of the infection. Between 20 and 57 per cent of surviving children develop long-term complications including limb amputation, cerebral infarction and skin scarring. We know little about the consequences of IMD in Australia.

PAEDS aims to examine records of children hospitalised with IMD to provide data on clinical features, severity of disease and outcomes associated with different meningococcal genotypes.

A health costing model will be developed from information collected by PAEDS on long-term outcomes in children hospitalised from IMD. Surveillance may also have the capacity to estimate vaccine effectiveness (against meningococcal B and all IMD).

Invasive group A streptococcal (IGAS) disease

Surveillance of invasive group A streptococcal (IGAS) disease began as a pilot at The Royal Children's Hospital in Melbourne in 2015. It is now being rolled out to all PAEDS sites in 2016.

The group A streptococcus (GAS) bacteria is a common infective agent in children and adults that causes the widest range of clinical disease in humans of any bacterium. The spectrum of GAS disease can be divided into superficial, invasive, toxin-mediated and post-infectious. The most common infections caused by GAS are superficial, such as pharyngitis and pyoderma, which predominantly affect children. Invasive diseases are less common but have high rates of mortality and long-term morbidity. They include bacteraemia, necrotising fasciitis and meningitis.

Currently there is no vaccine to prevent invasive group A streptococcal infection. The streptococcal M protein that is used as the substrate for epidemiological typing is the major virulence factor of group A streptococcus and is a key vaccine target. Over 220 variants of this protein have been described.

The aims of this project are:

1. To determine the incidence of invasive group A streptococcal disease, with special emphasis on the duration of hospitalisation, use of intensive care, death and disability.
2. To establish an ongoing surveillance system for hospitalised group A streptococcal disease.
3. To describe the clinical features of patients presenting with invasive group A streptococcal disease.
4. To genotypically characterise group A streptococcal isolates from patients with invasive group A streptococcal disease.

Welcome to new staff

The PAEDS network welcomes the following new staff members:

The Coordinating Centre at NCIRS

Nicole Dinsmore is a registered nurse with postgraduate qualifications and a background in paediatrics, specialising in caring for children with heart disease. She has experience in nursing education and an interest in public health issues. She joined the PAEDS network after she discovered a passion for furthering her knowledge in research, following the development of a nursing led clinical trial in The Heart Centre for Children.

Gemma Saravanos is a registered nurse with an interest in infectious diseases and a passion for public health research. She has completed postgraduate qualifications in immunisation and has been involved in the delivery of seasonal influenza vaccination clinics. Additionally she has completed her Honours in Biomedical Science and has been involved in research spanning medical diagnostics, immunisation and infectious diseases. Gemma is excited to contribute to the PAEDS team while spending time with her energetic toddler on days off.

Kathryn Meredith has been a registered nurse in neonatal intensive care for 21 years, working in the Grace Centre for Newborn Care for most of the last 15 years. She has worked for the last five years on the nursing casual pool, travelling around the wards at The Children's Hospital at Westmead. Having a natural curiosity, she has enjoyed being introduced to the world of surveillance and research and is enjoying being part of the awesome PAEDS team.

Stoy Drinic is a project officer with over 10 years experience in research administration and management gained at funding agencies and in the university sector. She has recently joined NCIRS to provide support and assistance in managing the grant and contract activities of the Centre. She is a very welcome addition to the PAEDS team at the Coordinating Centre.

Samantha Carlson is a social science research officer at NCIRS and has recently commenced a full-time Doctor of Philosophy (Medicine) under the co-primary supervision of CIA Kristine Macartney and CID Julie Leask, based on the PAEDS NHMRC-funded partnership project. Samantha has a Bachelor of Science (Immunobiology and Microbiology) and a Master of Public Health. Her PhD work will use the social ecological model of health to examine how interconnected systems (policy, community, organisational, interpersonal and intrapersonal) influence the development of severe influenza and pertussis in children. Samantha is excited to learn from and collaborate with all those involved in the PAEDS project.

Royal Darwin Hospital

Heather Cook is a registered nurse with postgraduate public health qualifications working at the Centre for Disease Control in Darwin. She has several years of experience within vaccine preventable disease surveillance and will provide valuable support and assistance in the roll-out of the PAEDS project within the Royal Darwin Hospital.

PAEDS publications* (2015-2016)

* This list includes all recent primary PAEDS publications and selected studies that include PAEDS data or are related to PAEDS studies. For a full list of all PAEDS publications please visit our website (paeds.edu.au).

- Zurynski YA, McRae J, Quinn HE, Wood NJ, Macartney K. Paediatric Active Enhanced Disease Surveillance (PAEDS) inaugural report 2014: prospective hospital-based surveillance for select vaccine preventable diseases and adverse events following immunisation. Communicable Diseases Intelligence 2016 [In press].
- Li-Kim-Moy J, Dastouri F, Rashid H, Khandaker G, Kesson A, McCaskill M, Wood N, Jones C, Zurynski Y, Macartney K, Elliott EJ, Booy R. Utility of early influenza diagnosis through point-of-care testing in children presenting to an emergency department. Journal of Paediatrics and Child Health 2016;52:422-9.
- Britton PN, Dale RC, Elliott E, Festa M, Macartney K, Booy R, Jones CA. Pilot surveillance for childhood encephalitis in Australia using the Paediatric Active Enhanced Disease Surveillance (PAEDS) network. Epidemiology and Infection 2016;144:2117-27.
- Khandaker G, Jung J, Britton PN, King C, Yin JK, Jones CA. Long-term outcomes of infective encephalitis in children: a systematic review and meta-analysis. Developmental Medicine and Child Neurology 2016;58:1108-15.
- Teoh HL, Mohammad SS, Britton PN, Kandula T, Lorentzos MS, Booy R, Jones CA, Rawlinson W, Ramachandran V, Rodriguez ML, Andrews PI, Dale RC, Farrar MA, Sampaio H. Clinical characteristics and functional motor outcomes of enterovirus 71 neurological disease in children. JAMA Neurology 2016;73:300-7.
- Blyth CC, Macartney KK, Hewagama S, Senenayake S, Friedman ND, Simpson G, Upham J, Kotsimbos T, Kelly P, Cheng AC. Influenza epidemiology, vaccine coverage and vaccine effectiveness in children admitted to sentinel Australian hospitals in 2014: the Influenza Complications Alert Network (FluCan). Eurosurveillance 2016;21(30):pii=30301.
- Britton PN, Dale RC, Nissen MD, Crawford N, Elliott E, Macartney K, Khandaker G, Booy R, Jones CA. Parechovirus encephalitis and neurodevelopmental outcomes. Pediatrics 2016;137:e20152848.
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- Britton PN, Eastwood K, Paterson B, Durrheim DN, Dale RC, Cheng AC, Kenedi C, Brew BJ, Burrow J, Nagree Y, Leman P, Smith DW, Read K, Booy R, Jones CA. Consensus guidelines for the investigation and management of encephalitis in adults and children in Australia and New Zealand. Internal Medicine Journal 2015;45:563-76.
- Britton PN, Eastwood K, Brew BJ, Nagree Y, Jones CA. Consensus guidelines for the investigation and management of encephalitis. Medical Journal of Australia 2015;202:576-7.
- Macartney KK, Gidding HF, Trinh L, Wang H, McRae J, Crawford N, Gold M, Kynaston A, Blyth C, Zurynski Y, Elliott E, Booy R, Buttery J, Marshall H, Nissen M, Richmond P, McInytre PB, Wood N. Febrile seizures following measles and varicella vaccines in young children in Australia. Vaccine 2015;33:1412-7.

Important events

PAEDS face-to-face annual meeting 2016

Our annual PAEDS face-to-face meeting was held at the North Sydney Harbourview Hotel on 16 and 17 March 2016.

The meeting was attended by PAEDS staff, investigators, nurses (from all sites) and PAEDS stakeholder representatives from NSW, South Australia, Queensland and Victoria Departments of Health and the Australian Government Department of Health.

The meeting was held over two days, commencing on day one with the PAEDS Surveillance Nurses Meeting followed by the PAEDS Investigators/Nurses Meeting. Day two was a full day involving the whole PAEDS team and representatives from our partnering and funding organisations. A range of issues were discussed in depth with excellent contributions from all in attendance.

PAEDS new annual report in *Communicable Diseases Intelligence*

In 2016, PAEDS submitted its inaugural report to *Communicable Diseases Intelligence*. This paper presents data obtained by PAEDS since inception in 2007 through to 2014 including results and impacts of surveillance on all conditions.

Upcoming announcements

Stay tuned for the location and dates of our next annual PAEDS face-to-face meeting, as well as our 2017 10-year anniversary celebrations. Plans are to hold the meeting in Sydney and in another state each alternate year.

Once details have been confirmed a 'save the date' will be posted on the PAEDS website.

For more information

Visit our website: paeds.edu.au

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You may also like to visit the NCIRS (ncirs.edu.au) or APSU (apsu.org.au) websites.

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