Surveillance of adverse events following immunisation in Australia annual report, 2014

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Abstract

This report summarises Australian passive surveillance data for adverse events following immunisation (AEFI) for 2014 reported to the Therapeutic Goods Administration for 2014 and describes reporting trends over the 15-year period 1 January 2000 to 31 December 2014. There were 3,087 AEFI records for vaccines administered in 2014; an annual AEFI reporting rate of 13.2 per 100,000 population. There was a decline of 5% in the overall AEFI reporting rate in 2014 compared with 2013. This decline in reported adverse events in 2014 compared with the previous year was mainly attributable to fewer reports following the human papillomavirus (HPV) vaccine as it was the 2nd year of the extension of the National HPV Vaccination Program to males. AEFI reporting rates for most vaccines were lower in 2014 compared with 2013. The most commonly reported reactions were injection site reaction (27%), pyrexia (18%), rash (16%), vomiting (9%), headache (7%), and syncope (5%). The majority of AEFI reports described non-serious events while 7% (n=211) were classified as serious. There were 5 deaths reported with no clear causal relationship with vaccination found. *Commun Dis Intell* 2016;40(3):E377–E390.

Keywords: AEFI, adverse events, vaccines, surveillance, immunisation, vaccine

Introduction

This report summarises national passive surveillance data for adverse events following immunisation (AEFI) reported to the Therapeutic Goods Administration (TGA) by 28 February 2015. The report focuses on AEFI reported for vaccines administered during 2014 and trends in AEFI reporting over the 15-year period 1 January 2000–31 December 2014.

An adverse event following immunisation is defined as any untoward medical occurrence that follows immunisation and that does not necessarily have a causal relationship with the usage of the vaccine.[1] The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.[1]

Thus, AEFI may be caused by a vaccine(s) or may be coincidental. Adverse events may also include conditions that occur following the incorrect handling and/or administration of a vaccine(s). The post-marketing surveillance of AEFI is particularly important to detect signals of rare, late onset or unexpected events, which are difficult to detect in pre-registration vaccine trials.

Reports summarising national AEFI surveillance data have been published regularly since 2003.[2–13] Trends in reported adverse events following immunisation are heavily influenced by changes to vaccine funding and availability provided through the National Immunisation Program (NIP). These changes impact on the interpretation of trend data and have been described in detail in previous reports published regularly since 2003.[2–13] Table 1 shows the chronological listing of the changes.

Recent changes that impact on AEFI surveillance data presented in this report are:

- On 31 December 2013, the secondary school Year 7 hepatitis B vaccine catch-up program ceased.
- From January 2014, the hepatitis B vaccine was recommended to at-risk groups: household contacts and sexual partners of people living with hepatitis B; people who inject drugs or are on opioid substitution therapy; people living with hepatitis C; men who have sex with men; people living with HIV and prisoners and remandees.
- In February 2013, the National Human Papillomavirus Vaccination Program (quadrivalent HPV vaccine Gardasil®, CSL Biotherapies/ Merck & Co. Inc.) was extended to males aged 12–13 years through the school-based program, including a 2-year catch-up program for males aged 14–15 years until the end of 2014.
- On 14 August 2013, TGA included Bexsero® (4CMenB) on the Australian Register of Therapeutic Goods.[14] The vaccine is registered for use in people ≥2 months of age for the prevention of invasive disease caused by serogroup B meningococci.[14,15] It is available through purchase on the private market.[14,15] This vaccine is not funded under the NIP.[15]

Table 1: Changes to the Australian Standard Vaccination Schedule (2005–2014)[2–14]

Year	Intervention
2014	4vHPV catch-up program for males aged 14–15 years
2013	From 1 February 2013, 4vHPV was extended to males aged 12–13 years, delivered through a school-based program, with a catch-up program for males aged 14–15 years in 2013 and 2014. From July 2013, the 2nd dose of MMR vaccine, previously given at 4 years, was brought forward to 18 months of age and delivered as a combination MMRV vaccine. From July 2013, combined *Haemophilus influenzae* type b (Hib) and meningococcal serogroup C (MenC) vaccine, Menitorix®, was funded for infants aged 12 months. This combination vaccine replaced the single dose of monovalent meningococcal C conjugate vaccine (MenCCV) and booster dose of monovalent Hib vaccine previously scheduled at 12 months of age. At the end of December 2013, the secondary school Year 7 hepatitis B vaccine catch-up program ceased, as all younger age cohorts were eligible for infant immunisation under the NIP (commenced 2000).
2012	From 1 October 2012, a 4th dose of Prevenar 13®, (13vPCV, a 13-valent pneumococcal conjugate vaccine) was listed on the National Immunisation Program (NIP) for Indigenous children, aged 12–18 months, residing in Queensland, South Australia, Western Australia and the Northern Territory. This replaced the booster dose of Pneumovax23®, (23vPPV, a 23-valent pneumococcal polysaccharide vaccine) administered between 18 and 24 months of age for Indigenous children from these jurisdictions.
2011	From 1 July 2011, Prevenar 13® replaced Prevenar® on the NIP for children at 2, 4 and 6 months of age in all states and territories except the Northern Territory, which adopted 13vPCV from 1 October 2011. 1 October 2011 to 30 September 2012 – all children aged between 12 and 35 months who had completed a primary pneumococcal vaccination course with 7vPCV, were eligible to receive a free supplementary dose of Prevenar 13® On 25 March 2011, TGA issued a recall of Batch N3336 of the 23 valent pneumococcal polysaccharide vaccine 23vPPV, Pneumovax® 23. April 2011: health professionals were advised not to administer a 2nd or subsequent dose of Pneumovax 23 vaccine. December 2011 - Revised recommendations regarding which patients should be re-vaccinated under the NIP were provided.
2010	Annual vaccination with seasonal trivalent influenza vaccine (TIV, containing 3 influenza strains: A/H1N1, A/H3N2 and B) was funded under the NIP for people aged ≥6 months with medical risk factors (previously subsidised through the Pharmaceutical Benefits Scheme) and all Indigenous people aged ≥15 years (previously all Indigenous adults ≥50 years and 15–49 years with medical risk factors). On 23 April 2010, the use of the 2010 seasonal TIV in children <5 years of age was suspended by Australia's Chief Medical Officer due to an increased number of reports of fever and febrile convulsions post vaccination. A subsequent investigation identified that Fluvax® and Fluvax junior® (CSL Biotherapies), but neither of the other 2 available brands registered for use in young children, were associated with an unacceptably high risk of febrile convulsions. The recommendation to resume the use of seasonal influenza vaccine in children aged 6 months to 5 years, using brands other than Fluvax® and Fluvax junior®, was made in August 2010.
2009	By late 2009, all states and territories were using the single hexavalent DTPa-IPV-Hib-HepB (Infanrix hexa®) vaccine for all children at 2, 4 and 6 months of age, due to an international shortage of *Haemophilus influenzae* type b (Hib) (PedvaxHib® [monovalent] and Comvax® [Hib-HepB]) vaccines. Pandemic H1N1 2009 influenza vaccine (Panvax®) was rolled out across Australia from 30 September 2009 for people aged ≥10 years. From December 2009, the pandemic vaccine was made available to children aged 6 months to 10 years.
2008	Western Australia commenced a seasonal influenza vaccination program for all children aged 6 months to <5 years (born after 1 April 2003). In March 2008, Queensland, South Australia and Victoria changed from using 2 combination vaccines (quadrivalent DTPa-IPV and Hib-HepB) to the single hexavalent DTPa-IPV-HepB-Hib vaccine.
2007	From April 2007, funded immunisation against human papillomavirus for all Australian girls aged 12–13 years delivered through a school-based program from April 2007, with a temporary catch-up program through schools or primary care providers for females aged 13–26 years until December 2009. From July 2007, universal funded immunisation against rotavirus at 2 and 4 months of age (Rotarix®) or at 2, 4 and 6 months of age (Rotateq®).
2005	From January 2005, universal funded infant 7-valent pneumococcal conjugate vaccine (7vPCV) program replaced the previous targeted childhood program, with a catch-up program for children aged <2 years. Universal 23vPPV for adults aged ≥65 years replaced previous subsidy through the Pharmaceutical Benefits Scheme. From November 2005, universal funded immunisation against varicella at 18 months of age with a school-based catch-up program for children at 10–13 years of age not previously vaccinated and without a history of varicella infection (no funded catch-up for children 2–10 years of age). Inactivated polio vaccine was funded to replace the oral polio vaccine, in combination vaccines.

A glossary of the abbreviations of the vaccines is include at the end of this report to assist readers.

Methods

AEFI are notified to the TGA by state and territory health departments, health professionals, vaccine companies and members of the public.[16,17] All reports are assessed using internationally consistent criteria[18] and entered into the Australian Adverse Drug Reactions System (ADRS) database. The TGA medical officers review all serious reports for drugs and vaccines. Reports are used in data mining and signal detection activities. Where there is insufficient information in a report to determine causality for a serious adverse event the TGA will contact the reporter on up to 3 occasions to elicit further information.

Adverse events following immunisation data

De-identified information on all AEFI reported to the TGA from 1 January 2000 to 31 December 2014 and stored in the ADRS database, were released to the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS) in March 2015. Readers are referred to previous AEFI surveillance reports for a description of the surveillance system.[2,5]

Records* contained in the ADRS database were eligible for inclusion in the analysis if a vaccine was recorded as 'suspected'† of involvement in the reported adverse event and *either*

a. the vaccination occurred between 1 January 2000 and 31 December 2014, *or*
b. for records where the vaccination date was not recorded, the date of onset of symptoms or signs that occurred between 1 January 2000 and 31 December 2014.

Study definitions of adverse events following immunisation

AEFI were defined as 'serious' or 'non-serious' based on information in the report sent to the TGA and criteria similar to those used by the World Health Organization[18] and the US Vaccine Adverse Events Reporting System.[19] In this report, an AEFI is defined as 'serious' if it meets one or more of the following criteria: (1) results in death; (2) is life-threatening; (3) requires inpatient hospitalisation or prolongation of existing hospitalisation; (4) results in persistent or significant disability/incapacity; (5) is a congenital anomaly/birth defect or; (6) is a medically important event or reaction.

Typically, each record lists several reaction terms that are symptoms, signs and/or diagnoses that have been coded by TGA staff from the reporter's description into standardised terms using the Medical Dictionary for Regulatory Activities (MedDRA®).[20,21]

In reports published previously, in order to analyse the data, MedDRA® coding terms were grouped to create a set of reaction categories that were broadly analogous to the reactions listed in previous *Australian Immunisation Handbooks*.[16,17] However, the methodological framework of reporting of adverse events have been reviewed by NCIRS in collaboration with TGA and a revised format for AEFI analyses using MedDRA preferred terms (PTs) was adopted.[22] For this report, MedDRA PTs are used for data analysis. Grouping of reactions using PTs is more comparable with data from other countries and internationally accepted.[23,24,25] In conjunction with the more recent national vaccine-specific reporting form,26 the use of PTs allow better reflection of post-marketing surveillance data on vaccines in Australia.

Data analysis

All data analyses were performed using SAS software version 9.3.[27] Average annual population-based reporting rates were calculated for each state and territory and by age group using 2014 population estimates obtained from the Australian Bureau of Statistics.[28] All rates are presented as average annual rates per 100,000 population. Reporting rates per 100,000 administered doses were estimated where information was available on the number of doses administered. This was done for vaccines funded through the NIP for children aged <7 years. The number of administered doses of each of the childhood vaccines was obtained from the Australian Childhood Immunisation Register (ACIR), a national population-based register of approximately 99% of children aged under 7 years.[29]

Notes on interpretation

Caution is required when interpreting the data presented in this report. Due to reporting delays and late onset of some AEFI, the data are considered preliminary, particularly for the 4th quarter of 2014. Data published in previous reports for 2000 to 2013

* The term 'AEFI record' is used throughout this report because a single AEFI notification/report to the Office of Product review can generate more than 1 record in the ADRS database. This may occur if there is a time sequence of separate adverse reactions in a single patient, such as systemic and local reactions.

† Vaccines are classified as 'suspected' if the report contains sufficient information to be valid and the relationship between reported reactions and the vaccine is deemed at least possible.

may differ from that presented in this report for the same period because this report has been updated to include delayed notifications to the TGA that were not included in prior publications. Data can also differ because reports may be updated and recoded when follow-up information is received or when vaccine-specific analyses are conducted.

The information collated in the ADRS database is intended primarily for signal detection and hypothesis generation. While reporting rates can be estimated using appropriate denominators, they cannot be interpreted as incidence rates due to under-reporting and biased reporting of suspected events, and the variable quality and completeness of information provided in individual notifications.[2–13,30]

It is important to note that this report is based on vaccine information and MedDRA preferred terms collated in the ADRS database and not on comprehensive clinical notes or case reviews. The reported symptoms, signs and diagnoses in each AEFI record in the ADRS database are temporally associated with vaccination but are not necessarily causally associated with a vaccine or vaccines.

Comparison with online Database of Adverse Events Notifications

In August 2012, the TGA made available to the public on its website a searchable database, the Database of Adverse Event Notifications (DAEN) that contains reports of all adverse event reports for medicines and vaccines.[31] The data in this report have not been downloaded from DAEN. This annual report uses data sent to NCIRS from the ADRS database by TGA in March 2015, and includes more detailed data than are provided by DAEN. The numbers published in this report may be different to the numbers in the DAEN database, due to different dates of data extraction and amendment to reports where further information has become available. In addition, this report provides several features that are not available from the DAEN database, including long-term trends and population and dose-based reporting rates, put in the context of changes in vaccine policy and use, and reporting practices.

Results

The ADRS database included a total of 3,087 records where the date of vaccination (or onset of adverse event, if vaccination date was not reported) was between 1 January and 31 December 2014.

In 2014, 82% of AEFI (n=2,521) were reported to the TGA via states and territories, while the rest were reported directly to the TGA by healthcare professionals (12% n=355), members of the public (4% n=119), vaccine companies (3% n=88) and hospitals (1% n=43).

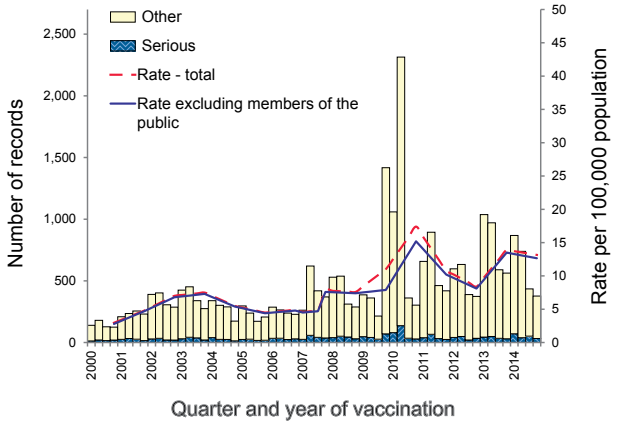
Reporting trends

The overall reporting rate for 2014 was 13.2 per 100,000 population compared with 13.9 per 100,000 in 2013. The highest peak was observed in 2010 (17.4 per 100,000) predominantly due to reports in children following vaccination with the pandemic and 2010 seasonal trivalent influenza vaccines.[11]

The vast majority of reported events in 2014 (from all reporter types) were of a non-serious nature similar to the previous years (Figure 1).[9,10] Figures 2a, 2b and 2c demonstrate marked variations in reporting levels in association with previous changes to the NIP from 2000 onwards. The decrease in reports in 2014 was predominantly due to a decline in reports following HPV vaccines in adolescents, and cessation of the hepatitis B program in schools (Figure 2c).

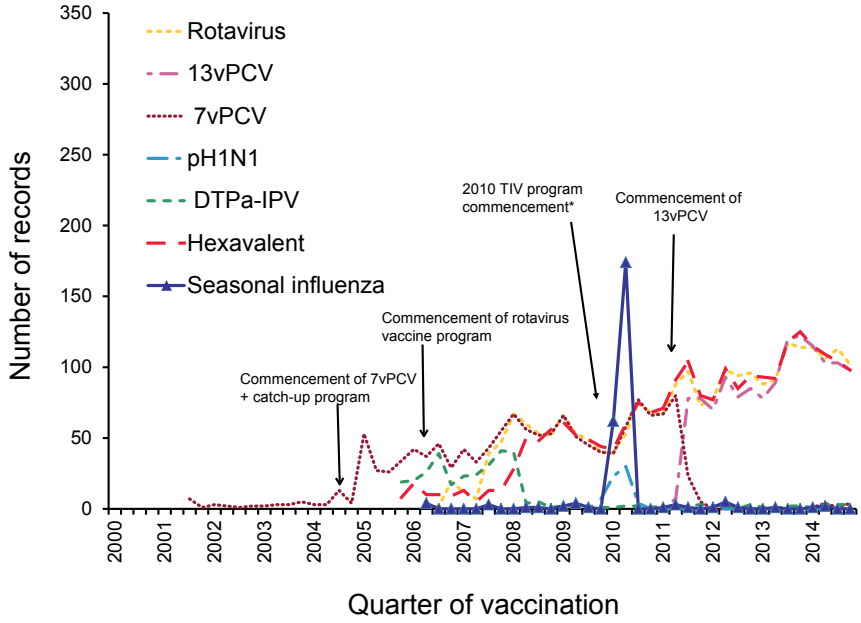
A seasonal pattern of AEFI reporting was apparent in 2014 as in previous years, with the highest number of AEFI notifications for vaccinations administered in the 1st half of the year (Figure 1). This corresponds with the months when influenza vaccine was given and older Australians received 23vPPV (March to June). However, more AEFI reports following influenza vaccine were received in each of the last 5 years than years prior to 2009 (pre-pandemic era) (Figure 2c).

Figure 1: Adverse events following immunisation, ADRS database, 2000 to 2014, by quarter and year of vaccination



For reports where the date of vaccination was not recorded, the date of onset or date event was reported to the Therapeutic Goods Administration was used as a proxy for vaccination date.

Figure 2a: Adverse events following immunisation for children aged <1 year, ADRS database, 2000 to 2014, by quarter and year of vaccination

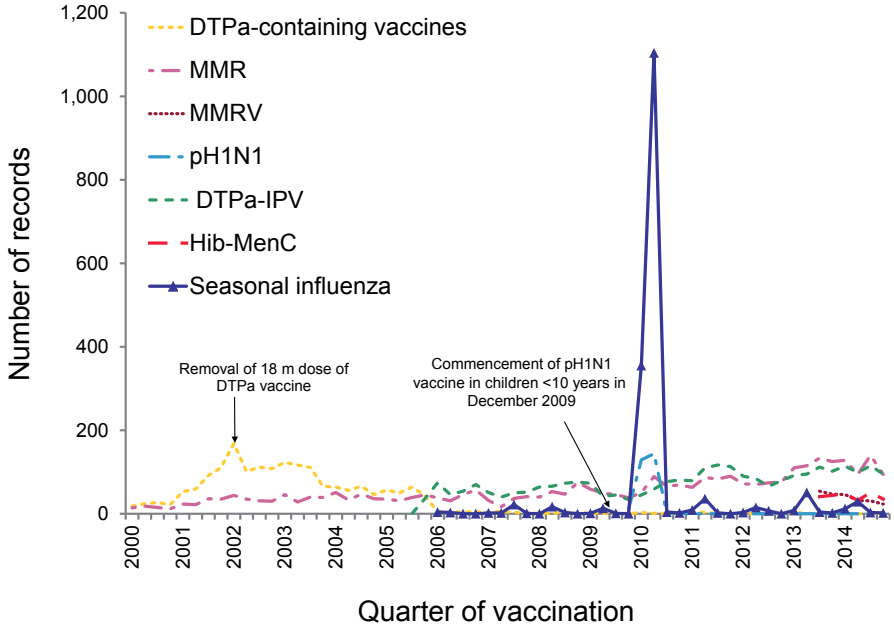


* Safety signal for fever and febrile convulsion found to be due to Seqirus, formerly bioCSL Fluvax 2010 TIV in children.

DTPa-IPV and DTPa-IPV-HepB-Hib (hexavalent) vaccines were introduced into the National Immunisation Program schedule in November 2005; rotavirus (RotaTeq® and Rotarix®) vaccines on 1 July 2007; pH1N1 influenza vaccine for children 6 months to 10 years on December 2009; seasonal trivalent influenza vaccine in 2010, which was an extension of existing adult and Indigenous programs to at-risk populations; and the 13-valent pneumococcal conjugate vaccine (13vPCV) on 1 July 2011 (Table 1).

For reports where the date of vaccination was not recorded, the date of onset or date event was reported to the Therapeutic Goods Administration was used as a proxy for vaccination date.

Figure 2b: Adverse events following immunisation for children aged 1 to <7 years in frequently reported vaccines, ADRS database, 2000 to 2014, by quarter and year of vaccination



* Safety signal for fever and febrile convulsion found to be due to Seqirus, formerly bioCSL, Fluvax 2010 TIV in children.

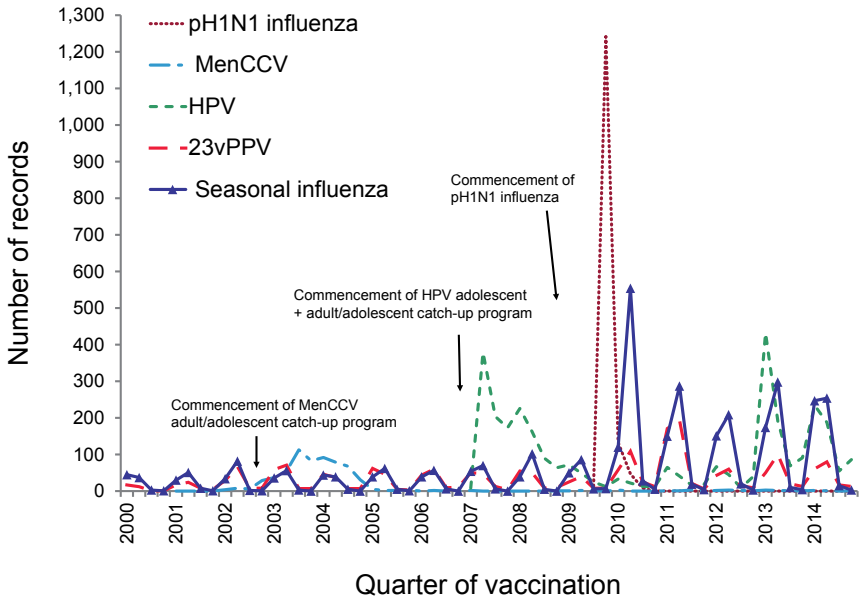
DTPa-IPV was introduced into the National Immunisation Program schedule in November 2005 replacing DTPa and OPV; seasonal trivalent influenza vaccine in 2010, which was an extension of existing adult and Indigenous programs to at-risk populations; MMRV and HibMenC vaccines on July 2013, and HPV program extended to boys in February 2013 (Table 1).

For reports where the date of vaccination was not recorded, the date of onset or date event was reported to the Therapeutic Goods Administration was used as a proxy for vaccination date.

Age distribution

The highest population-based AEFI reporting rate per 100,000 population occurred in infants under 1 year of age, the age group that received the highest number of vaccines (Figure 3). Compared with 2013, AEFI reporting rates in children decreased in the 1–<2 years age group from 132.1 to 117.3. A decline was also observed in the 7–<20 years age group from 26.6 to 19.7 (Figure 3).

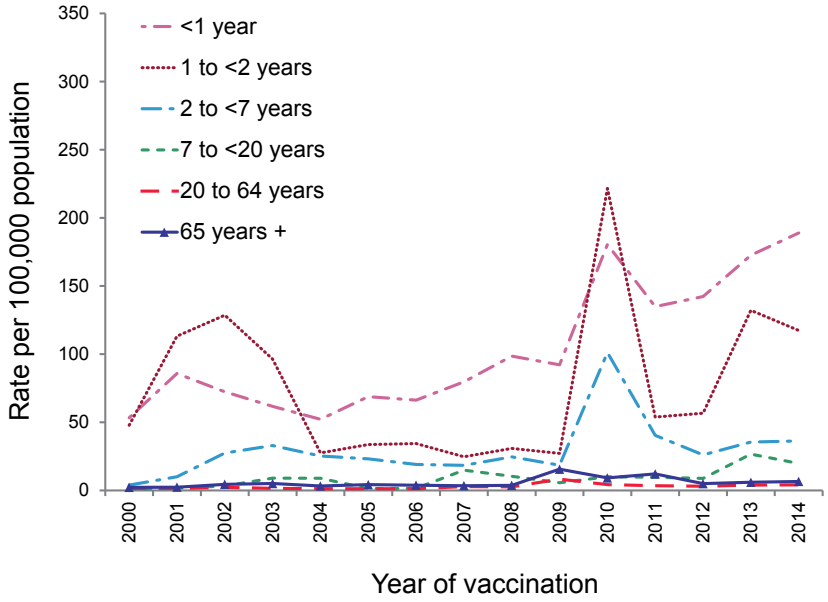
Figure 2c. Adverse events following immunisation for people aged ≥7 years in frequently reported vaccines, ADRS database, 2000–2014, by quarter of vaccination



MenCCVwas introduced into the National Immunisation Program schedule on 1 January 2003; pH1N1 influenza vaccine for children 6 months to 10 years on December 2009; pH1N1 vaccination for those ≥10 years commenced on 30 September 2009; seasonal trivalent influenza vaccine in 2010, which was an extension of existing adult and Indigenous programs to at-risk populations; and HPV program extended to boys in February 2013 (Table 1).

For reports where the date of vaccination was not recorded, the date of onset or date event was reported to the Therapeutic Goods Administration was used as a proxy for vaccination date.

Figure 3: Reporting rates of adverse events following immunisation per 100,000 population, ADRS database, 2000 to 2014, by age group and year of vaccination



For reports where the date of vaccination was not recorded, the date of onset or date event was reported to the Therapeutic Goods Administration was used as a proxy for vaccination date.

Reporting rates per 100,000 doses decreased overall and for most individual vaccines in 2014 compared with 2013 (Table 2). For children under 7 years of age, rates for varicella and MenC should be interpreted with caution since these monovalent vaccines were replaced by combination vaccines in July 2013 and hence very few doses were given during 2014.

Geographical distribution

Population-based reporting patterns varied between states and territories during 2014 (Table 3) as in previous years.[2,–13] Reporting rates decreased in most jurisdictions in 2014 compared with 2013 except in Victoria and South Australia, which experienced a slight increase.

Table 2: Vaccine types listed as 'suspected' in records of adverse events following immunisation by age groups (<7, 7–17, 18–64 and ≥65 years), ADRS database, 2014

Vaccines*	AEFI records† (n)	Vaccine doses	Reporting rate per 100,000 doses§ 2014 Rate	2014 95% CI	2013 Rate	2013 95% CI
<7 years						
DTPa-containing vaccines	894	1,169,168	76.5	71.6–81.6	75.2	70.3–80.3
Hexavalent (DTPa-IPV-HepB-Hib)	461	866,828	53.2	48.5–58.3	53.7	49.0–58.9
DTPa-IPV	433	302,340	143.2	130.3–157.4	136.7	123.8–150.7
Measles-mumps-rubella	480	594,553	80.7	73.8–88.3	83.6	76.4–91.2
Pneumococcal conjugate – PCV	450	880,999	51.1	46.6–56.0	52.8	48.1–57.9
Rotavirus vaccine	442	716,984	61.6	56.2–67.7	77.2	70.0–85.0
Meningococcal C conjugate	13	10,476	124.1	72.1–213.7	57.9	47.5–70.0
Measles-mumps-rubella-varicella	138	301,203	45.8	38.8–54.1	75.1	61.3–91.1
Haemophilus influenzae type b	5	12,943	38.6	16.1–92.8	56.2	45.5–68.6
Hib–MenC	180	295,170	61.0	52.7–70.6	73.7	59.4–90.3
Seasonal influenza	49	n/a	–		–	
Varicella	11	11,586	94.9	52.6–171.4	37.4	28.5–48.1
Total (<7 years)	1,485	4,002,987	37.1	35.3–39.0	36.1	34.3–38.1
7–17 years						
HPV	556	n/a	–		–	
Hepatitis B	4	n/a	–		–	
dTpa	216	n/a	–		–	
Varicella	112	n/a	–		–	
Seasonal influenza	32	n/a	–		–	
Total (7–17 years)	729	n/a	–		–	
18–64 years						
Seasonal influenza	374	n/a	–		10.5	9.4–11.7
dTpa	53	n/a	–		–	
23vPPV	39	n/a	–		42.3	31.9–54.9
Total (18–64 years)	582	n/a	–		11.8	10.7–13.0
≥65 years						
Seasonal influenza	113	n/a	–		4.3	3.5–5.2
23vPPV	120	n/a	–		35.9	29.6–43.1
dTpa	6	n/a	–		–	
Total (≥65 years)	226		–		8.3	7.2–9.5

* Records where at least 1 of the vaccines shown in the table was suspected of involvement in the reported adverse event.

† Number of adverse events following immunisation records in which the vaccine was coded as 'suspected' of involvement in the reported adverse event and the vaccination was administered between 1 January and 31 December 2014. More than 1 vaccine may be coded as 'suspected' if several were administered at the same time.

‡ Number of vaccine doses recorded on the Australian Childhood Immunisation Register and administered between 1 January and 31 December 2014.

§ The estimated reporting rate per 100,000 vaccine doses recorded.

n/a Not applicable.

Vaccines

There were 3,087 AEFI records received in 2014 (Table 4). The percentage of records where only 1 vaccine was reported as being the suspected vaccine differed by vaccine administered, typically varying according to whether multiple vaccines were routinely co-administered for the patient's age. There were slight variations in the numbers with events defined as 'serious', which have remained low as in previous years.

The most frequently reported individual vaccine was seasonal influenza vaccine with 589 records (19%), followed by HPV vaccine with 571 records (18.5%), MMR (n=523; 17%), hexavalent DTPa-IPV-HepB-Hib (n=467; 15%) and rotavirus vaccine (n=446; 14%) (Table 4).

For HPV vaccine, of the 571 AEFI reports, 57% were reported in males and 43% in females (Figure 4). HPV vaccine was the only suspected vaccine in 334 records (58.5%).

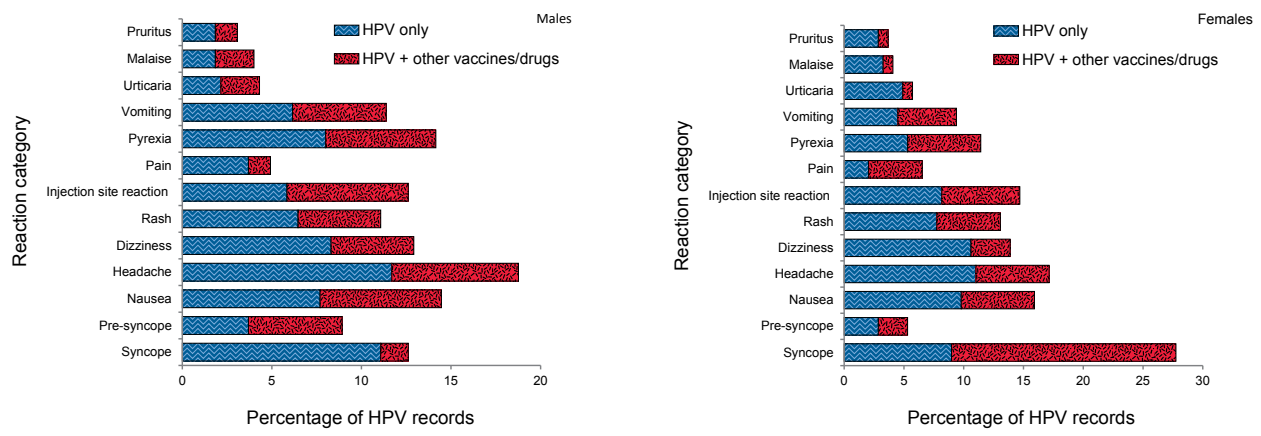
Table 3: Adverse events following immunisation records, ADRS database, 1 January to 31 December 2014, by state or territory

State or territory	AEFI records n	%	Annual reporting rate per 100,000 population* 'Serious'†	Aged <7 years	Overall rate	95% confidence interval
Australian Capital Territory	164	5.3	1.3	8.0	42.5	36.5–49.5
New South Wales	518	16.8	0.7	2.4	6.9	6.3–7.5
Northern Territory	52	1.7	2.0	7.3	21.2	16.2–27.8
Queensland	574	18.6	0.5	5.8	12.2	11.2–13.2
South Australia	280	9.1	0.8	6.8	16.6	14.8–18.7
Tasmania	82	2.7	0.2	6.0	15.9	12.8–19.8
Victoria	1212	39.3	1.6	12.3	20.8	19.6–22.0
Western Australia	205	6.6	0.7	4.4	8.0	6.9–9.1
Total	3,087	100.0	0.9	6.3	13.2	12.7–13.6

* Average annual rates per 100,000 population calculated using Australian Bureau of Statistics mid-2014 population estimates.

† Adverse events following immunisation records defined as 'serious' (i.e. recovery with sequelae, hospitalisation, life-threatening or death).

Figure 4: Most frequently reported adverse events following immunisation with human papillomavirus vaccine,* 2014, by number of vaccines suspected of involvement in the reported adverse event



* Per cent of 325 adverse events following immunisation records (human papillomavirus males) and 245 records (human papillomavirus females) where the vaccine was listed as suspected of involvement in the reported adverse event following immunisation.

Source: Adverse Drug Reactions Reporting System database, Therapeutic Goods Administration.

Table 4: Vaccine types listed as 'suspected' in records of adverse events following immunisation, ADRS database, 2014

Suspected vaccine type	AEFI records		One suspected vaccine only†		'Serious'§		<7 years‖		≥7 years ‖	
	n	%	n	%¶	n	%¶	n	%¶	n	%¶
Influenza	589	19.1	495	84.0	32	5.4	49	8.3	541	91.7
HPV	571	18.5	334	58.5	31	5.4	2	0.4	569	99.6
MMR	523	16.9	103	19.7	35	6.7	480	91.8	38	7.3
DTPa-IPV-HepB-Hib	467	15.1	36	7.7	49	10.5	461	98.7	3	0.6
Rotavirus	446	14.4	61	13.7	56	12.6	442	99.1	1	0.2
13vPCV	445	14.4	13	2.9	49	11.0	439	98.7	6	1.3
DTPa-IPV	443	14.3	203	45.8	14	3.2	433	97.7	8	1.8
dTpa	281	9.1	131	46.6	9	3.2	3	1.1	278	98.9
23vPPV	185	6.0	116	62.7	6	3.2	7	3.8	178	96.2
Hib-MenC	181	5.9	9	5.0	22	12.2	180	99.4	1	0.6
MMRV	140	4.5	119	85.0	20	14.3	138	98.6	2	1.4
Varicella	138	4.5	26	18.8	2	1.4	11	8.0	124	89.9
Meningococcal B	66	2.1	64	97.0	2	3.0	39	59.1	24	36.4
Hepatitis B	61	2.0	42	68.9	1	1.6	9	14.8	34	55.7
dT	22	0.7	18	81.8	2	9.1	0	0.0	22	100.0
Hepatitis A-Typhoid	20	0.6	11	55.0	0	0.0	1	5.0	19	95.0
BCG	19	0.6	18	94.7	1	5.3	17	89.5	1	5.3
Yellow fever	18	0.6	11	61.1	0	0.0	0	0.0	17	94.4
Hepatitis A	17	0.6	5	29.4	1	5.9	8	47.1	9	52.9
MenCCV	17	0.6	3	17.6	1	5.9	13	76.5	4	23.5
Typhoid	15	0.5	6	40.0	3	20.0	2	13.3	13	86.7
Rabies	12	0.4	9	75.0	0	0.0	0	0.0	12	100.0
Q fever	11	0.4	11	100.0	1	9.1	0	0.0	11	100.0
Zoster	9	0.3	8	88.9	1	11.1	0	0.0	9	100.0
Hib	7	0.2	0	0.0	0	0.0	5	71.4	2	28.6
Hepatitis A + B	6	0.2	4	66.7	1	16.7	0	0.0	6	100.0
Cholera	5	0.2	4	80.0	0	0.0	0	0.0	5	100.0
Japanese encephalitis	3	0.1	1	33.3	0	0.0	0	0.0	3	100.0
Tetanus	1	0.0	0	0.0	0	0.0	0	0.0	1	100.0
Total**	3,087	100.0	18,73	60.7	211	6.8	1,485	48.1	1,537	49.8

* Abbreviations of vaccine names are defined in the Appendix.

† Adverse events following immunisation (AEFI) records where only 1 vaccine was suspected of involvement in a reported adverse event.

‡ Causality ratings were assigned to AEFI records using criteria described previously.[2,3]

§ 'Serious' is defined in the Methods section.

‖ Includes only AEFI records where an age or date of birth has been reported.

¶ Percentages are calculated for the number of AEFI records where the vaccine was suspected of involvement in the AEFI.

** Total number of AEFI records analysed, not the total in each column as categories are not mutually exclusive and an AEFI record may list more than 1 vaccine.

Reactions

In 2014, there was a total of 6,810 events reported for 3,087 AEFI records. Out of the 3087 records, the most frequently reported adverse events were injection site reactions (ISRs) (n=832; 27%), pyrexia (n=558; 18%), rash (n=484; 16%), vomiting (n=289; 9%), headache (n=219; 7%), nausea (n=193; 6%), extensive swelling of vaccinated limb (n=177; 6%) and syncope (n=154; 5%) (Table 5, Figure 5). Some of the other reactions of interest were convulsions (n=85; 3%), hypotonic-hyporesponsive episode (n=51; 1.7%), intussusception (n=16; 0.5%) and

Guillain-Barré syndrome (n=5; 0.2%) (Table 5). Anaphylaxis (n=20) was reported for less than 1% of AEFI records in 2014.

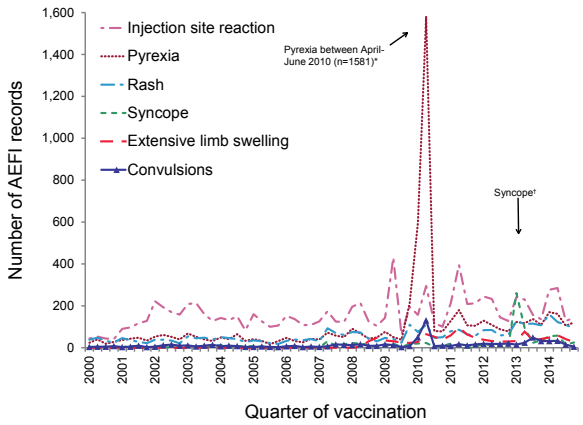
The number of reports for each reaction has changed over time (Figure 5). The variation in reporting of ISRs is related to changes in the immunisation schedule for vaccines that are known to have higher rates of ISR, including DTPa-containing vaccines, MenCCV, 23vPPV and HPV vaccine.[2–13,32,33] Increases in reports of fever were largely associated with time periods when new vaccines were added to the NIP in the reporting period, such as 7vPCV and HPV; the extension of seasonal influenza vaccine on the NIP to include persons <65 years at high risk of influenza in 2010; 13vPCV replacing 7vPCV in July 2011; and the extension of HPV to males in 2013.

For HPV vaccine, the spectrum of reactions was similar in boys and girls in this reporting period, however there were more cases in females of syncope (62% in females versus 38% in males) (Figure 4)

Severity

The majority of reported events in 2014 were defined as 'non-serious' and only 7% (n=211) were defined as 'serious'. This was similar to the proportions of serious AEFI in previous years.[9,11,12]

Figure 5: Selected frequently of reported adverse events following immunisation, ADRS database, 2000 to 2014, by quarter and year of vaccination



* Associated with administration of bioCSL Fluvax 2010 TIV and associated stimulated reporting.

† The peak in syncope coincided with the enhanced human papillomavirus surveillance program in which there was stimulated reporting of syncope for the first 6 months of 2013.

For reports where the date of vaccination was not recorded, the date of onset or date event was reported to the Therapeutic Goods Administration was used as a proxy for vaccination date. Also, grouping for reactions are different for this report though these reactions have been mapped back to 2000 as mentioned in the Methods section.

Table 5: Selected reported adverse events and reactions of interest* classified by MedDRA Preferred Terms in records of adverse events following immunisation, ADRS database, 2014

MedDRA preferred terms adverse events	AEFI records	Only reaction reported†		'Serious'‡		<7 years§		≥7 years§	
	N	n	%‖	n	%‖	n	%‖	n	%‖
Injection site reaction¶	832	360	43.3	8	1.0	397	47.7	422	50.7
Pyrexia	558	14	2.5	47	8.4	318	57.0	230	41.2
Rash**	484	185	38.2	29	6.0	325	67.1	153	31.6
Vomiting	289	30	10.4	32	11.1	166	57.4	120	41.5
Headache	219	4	1.8	9	4.1	8	3.7	209	95.4
Nausea	193	3	1.6	4	2.1	7	3.6	180	93.3
Extensive limb swelling	177	73	41.2	3	1.7	106	59.9	67	37.9
Syncope	154	117	76.0	8	5.2	17	11.0	135	87.7
Diarrhoea	153	11	7.2	16	10.5	114	74.5	39	25.5
Lethargy	145	0	0.0	11	7.6	62	42.8	82	56.6
Dizziness	142	11	7.7	4	2.8	1	0.7	136	95.8
Urticaria	139	57	41.0	6	4.3	72	51.8	65	46.8
Irritability	127	5	3.9	15	11.8	124	97.6	2	1.6
Pain	126	5	4.0	6	4.8	19	15.1	105	83.3
Malaise	105	1	1.0	4	3.8	11	10.5	92	87.6
Pallor	94	2	2.1	9	9.6	48	51.1	46	48.9
Erythema	85	15	17.6	1	1.2	39	45.9	46	54.1
Convulsions††	85	60	70.6	27	31.8	83	97.6	2	2.4

Table 5 continued: Selected reported adverse events and reactions of interest* classified by MedDRA Preferred Terms in records of adverse events following immunisation, ADRS database, 2014

MedDRA preferred terms adverse events	AEFI records	Only reaction reported†		'Serious'‡		<7 years§		≥7 years§	
	N	n	%‖	n	%‖	n	%‖	n	%‖
Myalgia	82	2	2.4	3	3.7	4	4.9	77	93.9
Pruritus	79	6	7.6	1	1.3	18	22.8	60	75.9
Decreased appetite	71	0	0.0	4	5.6	48	67.6	22	31.0
Presyncope	70	41	58.6	1	1.4	6	8.6	63	90.0
Abdominal pain	68	2	2.9	8	11.8	31	45.6	37	54.4
Fatigue	61	0	0.0	3	4.9	4	6.6	55	90.2
Cough	54	2	3.7	4	7.4	26	48.1	28	51.9
Paraesthesia	54	1	1.9	1	1.9	1	1.9	52	96.3
Chills	51	0	0.0	1	2.0	3	5.9	48	94.1
Hypotonic-hyporesponsive episode	51	34	66.7	10	19.6	50	98.0	0	0.0
Arthralgia	47	3	6.4	1	2.1	2	4.3	45	95.7
Somnolence	42	1	2.4	3	7.1	29	69.0	13	31.0
Dyspnoea	39	0	0.0	5	12.8	7	17.9	31	79.5
Hyperhidrosis	35	0	0.0	1	2.9	5	14.3	35	100.0
Oropharyngeal pain	30	1	3.3	0	0.0	6	20.0	24	80.0
Rhinorrhoea	28	0	0.0	3	10.7	20	71.4	8	28.6
Hypoaesthesia	27	2	7.4	1	3.7	0	0.0	27	100.0
Tachycardia	24	0	0.0	7	29.2	10	41.7	13	54.2
Haematochezia	22	6	27.3	3	13.6	21	95.5	1	4.5
Anaphylactic reaction	20	16	80.0	20	100.0	6	28.6	12	57.1
Tremor	16	2	12.5	0	0.0	4	25.0	11	68.8
Intussusception	16	13	81.3	7	43.8	16	100.0	0	0.0
Chest discomfort	16	0	0.0	1	6.3	0	0.0	15	93.8
Lymphadenitis	6	2	33.3	0	0.0	0	0.0	6	100.0
Guillain-Barré syndrome	5	3	60.0	3	60.0	0	0.0	3	60.0

* Selected reported adverse events reported during 1 January to 31 December 2014. For injection site reaction, rash and convulsions, Preferred Terms (PTs) were grouped as described below. A complete list of adverse reactions as classified by individual Preferred Terms is available on request.

† Adverse events following immunisation (AEFI) records where only one reaction was reported.

‡ 'Serious' is defined in the Methods section.

§ Includes only AEFI records where an age or date of birth has been reported.

‖ Percentages relate to the number of AEFI records in which the specific reaction term was listed.

¶ Injection site reaction includes the following MedDRA PTs: injection site reaction, injection site swelling, injection site pain, injection site mass, injection site erythema, injection site cellulitis, injection site rash, injection site induration, injection site abscess, injection site pruritus, injection site nodule, injected limb mobility decreased, injection site urticaria, injection site inflammation, injection site bruising, injection site infection, and injection site warmth.

** Rash includes the following MedDRA PTs: rash, rash generalised, rash erythematous, rash pruritic, rash maculo-papular, rash macular, rash vesicular, rash papular, rash morbilliform, and rash pustular.

†† Convulsion includes the following MedDRA PTs: febrile convulsion, and convulsion, grand mal convulsion, and partial seizures.

Five deaths were recorded as temporally associated with receipt of vaccines in 2014:

- A 77-year-old male immunised with a seasonal influenza vaccine died 9 hours later from sudden cardiac arrest. He had left ventricular dysfunction and a medical history of hypertension.
- A 58-year-old male had an infected leg wound prior to vaccination with diphtheria and tetanus vaccine and seasonal influenza vaccine. He developed acute disseminated myeloencephalitis, which progressed over 6 weeks leading to death. Symptom onset date was 5 days after vaccination.

- A 2-month-old female infant who had received Infanrix hexa®, Prevenar 13® and Rotateq® died 4 days following immunisation in hospital. *Bordetella pertussis* DNA was detected from the epiglottis on post-mortem.
- A 1-year-old male child in the terminal stages of spinal muscular atrophy type 1 died 7 days following vaccination with measles-mumps-rubella (Priorix®), seasonal influenza (Vaxigrip Junior®) and Hib–MenC (Menitorix®) vaccines.
- A 2-month old male infant died 2 days following immunisation with Infanrix hexa®, Prevenar 13® and Rotateq®. He had underlying congenital heart disease (atrio-ventricular septal defect and aortic arch repair with post-operative complications).

All deaths were investigated by the TGA and no clear causal relationship with vaccination was found.

Discussion

This report uses a similar methodology of analysis used in the previous 2013 annual report. As per the previous report, this method allows for clearer reporting of adverse events using MedDRA PTs, as used in the DAEN. This change in methodology needs to be taken into account when comparing with data from pre-2013 annual reports on specific reaction terms and categories.

In 2014, there was an overall decline in the AEFI reporting rate. The decline was likely due to it being the second year of the extension of National HPV Vaccination Program to males. There is usually an increase in reporting of adverse events when a program is newly rolled out. Historical data have shown that initial high levels of AEFI reporting occur each time a new vaccine is introduced, as immunisation providers are more likely to report milder, less serious AEFIs for vaccines with which they are not familiar, which is then followed by a reduction and stabilisation of reporting over time. Of note, during 2013 and 2014 the TGA, together with states and territories, closely monitored adverse events reported following HPV vaccination as the program was extended to males, including via enhanced surveillance using rapid reporting from school-based programs.[34]

Furthermore, in 2014, the drop in the number of adverse events could partially be attributed to ceasing the school-based hepatitis B vaccination program by the end of 2013 and therefore only 4 adverse events for hepatitis B vaccine were reported for this cohort of children. In addition, there were very few reports of adverse events following administration of monovalent vaccines such as varicella, MenC and Hib in this reporting period. This was anticipated as the combined Hib–MenC vaccine replaced the respective monovalent MenC and Hib vaccines in July 2013. Also, from July 2013, the 2nd dose of MMR vaccine was brought forward to 18 months of age and delivered as a combination MMRV vaccine.

Overall in Australia, injection site reaction, pyrexia and rash were the most commonly reported reactions in 2014. Vaccines such as DTPa-containing vaccines, MMR, rotavirus, Hib-MenC and pneumococcal conjugate (PCV13) had higher reporting rates than other vaccines for children aged under 7 years in the current reporting period. However, these rates were not significantly higher than the previous reporting period.

Conclusion

The total number of reported AEFI in 2014 decreased compared with 2013. The majority of AEFIs reported to the TGA were mild transient events. The data reported here are consistent with an overall high level of safety for vaccines included in the NIP schedule.

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Abbreviations of vaccine types

7vPCV	7-valent pneumococcal conjugate vaccine
13vPCV	13-valent pneumococcal conjugate vaccine
23vPPV	23-valent pneumococcal polysaccharide vaccine
BCG	Bacille Calmette-Guérin (i.e. tuberculosis)
dT	diphtheria-tetanus – adolescent and adult formulation
DTPa	diphtheria-tetanus-pertussis (acellular) – paediatric formulation
dTpa	diphtheria-tetanus-pertussis (acellular) – adolescent and adult formulation
DTPa-IPV	combined diphtheria-tetanus-pertussis (acellular) and inactivated poliovirus (quadrivalent)
DTPa-IPV-HepB-Hib	combined diphtheria-tetanus-pertussis (acellular), inactivated poliovirus, hepatitis B and *Haemophilus influenzae* type b vaccine (hexavalent)
HepB	hepatitis B
Hib	*Haemophilus influenzae* type b
Hib-HepB	combined *Haemophilus influenzae* type b and hepatitis B
Hib-MenC	combined Haemophilus influenzae type b and meningococcal C conjugate vaccine
HPV	human papillomavirus
MenCCV	meningococcal C conjugate vaccine
MMR	measles-mumps-rubella
MMRV	measles-mumps-rubella-varicella
pH1N1	pandemic H1N1 influenza 2009

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