Surveillance of adverse events following immunisation, NSW, 2012–2013

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Abstract: Aim: This report summarises passive surveillance data for adverse events following immunisation (AEFI) in NSW for a 2-year period from 1 January 2012 to 31 December 2013. **Methods:** Analysis of de-identified data on all adverse events following immunisation reported to the Therapeutic Goods Administration (TGA) for persons from NSW. **Results:** There were 973 AEFI reported for vaccines administered during 1 January 2012–31 December 2013. There was a decrease in reported adverse events in 2012 ($n = 330$) compared with 2011 ($n = 449$) mainly attributable to fewer reports following 23-valent pneumococcal polysaccharide vaccine (23vPPV) (145 reduced to 24). However, during 2013 the number of adverse events reported almost doubled ($n = 641$) due to implementation of enhanced vaccine safety reporting. This included enhanced reporting as part of the extension of the national HPV vaccination program to males from February 2013 ($n = 245$; includes 51% males and 49% females) and the increase in reports for children aged 1 to <2 years due to enhanced surveillance following MMRV and HibMenC, new vaccines on the National Immunisation Program (NIP) from July 2013. Overall, the most commonly reported reactions for both of the years were injection site reactions (24%), syncope (19%), and pyrexia and rash (12% each). Only 7% of the reported adverse events were categorised as serious. There were two reports of death; however, no clear causal relationship with vaccination was found after investigation by the TGA. **Conclusion:** Fluctuations in numbers of reports from 2012 and 2013 were observed, with increased reporting associated with enhancements to vaccine safety surveillance implemented for new NIP vaccines in 2013. However, no vaccine safety signals or concerns were observed in this 2-year period.

Abbreviations of vaccine types

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 dTpa and inactivated poliovirus
DTPa-HepB	combined diphtheria-tetanus-pertussis (acellular) and hepatitis B
DTPa-IPV	combined diphtheria-tetanus-pertussis (acellular) and inactivated poliovirus (quadrivalent)
DTPa-IPV-HepB	combined diphtheria-tetanus-pertussis (acellular), inactivated poliovirus and hepatitis B (pentavalent)
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
HibMenC	combined *Haemophilus influenzae* type b and meningococcal C vaccine
HPV	human papillomavirus
IPV	inactivated poliovirus vaccine
Men4PV	meningococcal polysaccharide tetravalent vaccine
MenCCV	meningococcal C conjugate vaccine
MMR	measles-mumps-rubella
MMRV	measles-mumps-rubella-varicella
7vPCV	7-valent pneumococcal conjugate vaccine
13vPCV	13-valent pneumococcal conjugate vaccine
23vPPV	23-valent pneumococcal polysaccharide vaccine

Introduction

This is the fifth in a series of annual reports of adverse events following immunisation (AEFI) in New South Wales (NSW). This report summarises passive surveillance data reported from NSW for the 2-year period 2012–2013, and describes reporting trends over the 14-year period 2000–2013.

An adverse event following immunisation is defined as any untoward medical occurrence that follows immunisation.[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-licensure surveillance of adverse events following immunisation is particularly important to detect rare, late onset and unexpected events, and new vaccine safety signals that are difficult to detect in pre-licensure vaccine trials.

Trends in reported adverse events following immunisation are heavily influenced by changes to vaccines provided through the National Immunisation Program (NIP). Changes in previous years have been reported elsewhere.[2–12] Recent changes that impact on AEFI surveillance data presented in this report are:

- In February 2013, the National HPV Vaccination Program (quadrivalent HPV vaccine Gardasil® – CSL Biotherapies/Merck & Co. Inc.) was extended to include 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.
- From July 2013, the second dose of MMR vaccine, previously given at 4 years, was brought forward to 18 months of age and delivered as a combination MMRV vaccine. MMR continues to be given at 4 years of age to children aged 19-48 months at 1 July 2013.
- From July 2013, combined *Haemophilus influenzae* type b (Hib) and meningococcal serogroup C (MenC) vaccine, Menitorix®, replaced the separate administration of monovalent meningococcal C conjugate vaccine (MenCCV) and Hib vaccine on the NIP at 12 months of age.

Methods

Adverse events following immunisation are notifiable to NSW public health units by medical practitioners and hospital CEOs under the NSW *Public Health Act 2010*. Cases with any outstanding information and all serious AEFI are followed up by public health units and Health Protection NSW. All notifications are forwarded to the Therapeutic Goods Administration (TGA). The TGA also receives reports directly from vaccine manufacturers, members of the public and other sources.[13,14]

Adverse events following immunisation data

Reports from all sources across Australia are assessed by the TGA using internationally consistent criteria[15] and entered into the Australian Adverse Drug Reaction Reporting System (ADRS) database. The term 'AEFI record' is used throughout this report because a single adverse event can result in more than one notification and generate more than one record in the ADRS database. This may occur if there is a time sequence of separate adverse reactions in a single patient.

Typically, each AEFI record lists several symptoms, signs and diagnoses that have been coded by TGA staff from the description provided by the reporter into standardised terms using the Medical Dictionary for Regulatory Activities (MedDRA®).[16]

In reports published previously,[8,9] analysis was conducted using MedDRA® terms grouped into 'reaction categories' that were broadly analogous to the reactions listed in previous *Australian Immunisation Handbooks*.[13,14] However, the methodological framework for reporting of adverse events has been recently revised by the National Centre for Immunisation Research and Surveillance (NCIRS) and the TGA. This new format for AEFI analyses uses MedDRA preferred terms (PTs)[17] for data analysis in this report. Therefore, presentation of data in previously published AEFI reports is different to this report. Grouping of reactions using PTs is more comparable with data from other countries and internationally accepted.[18–20] In conjunction with the new national vaccine-specific reporting form,[21] the use of PTs allows better description of post-marketing surveillance data on vaccine safety in Australia.

Definitions of adverse events following immunisation outcomes and reactions

This report includes only AEFI records that are classified as 'suspected' to be causally related to immunisation by medical officers within the TGA. An AEFI record is classified as 'not suspected' and excluded from the ADRS database if: (1) there is no reasonable temporal association between the use of a drug and the clinical event; (2) the record does not contain enough information for an adequate assessment or the information is contradictory; or (3) if a clinical event is explained as likely to have arisen from other causes.

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[16] and the US Vaccine Adverse Events Reporting System (VAERS).[22] 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;

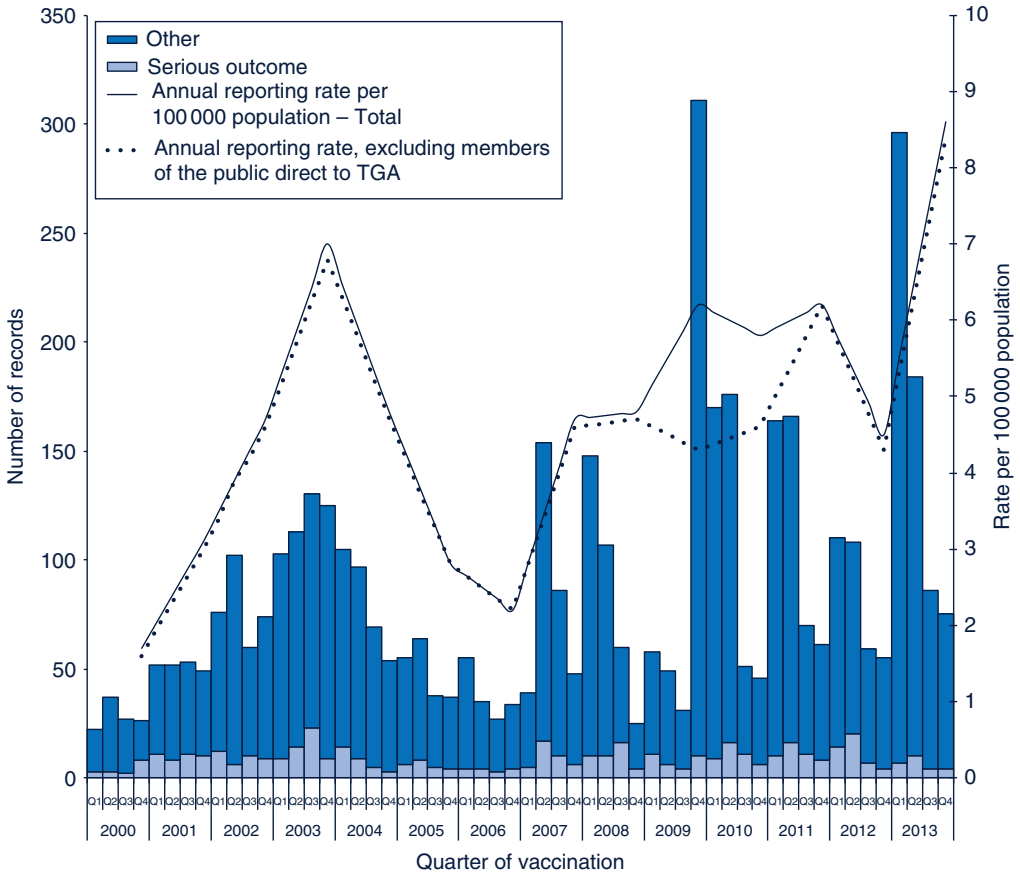

Figure 1. Reports of adverse events following immunisation, NSW, 2000–2013, by quarter of vaccination.

NB: For reports where the date of vaccination was not recorded, the date of onset was used as a proxy for vaccination date.

Source: Adverse Drug Reactions Reporting System database, TGA.

(5) is a congenital anomaly/birth defect; and/or (6) is a medically important event or reaction.

Data analysis

De-identified information on AEFI reports from the ADRS database was released to NCIRS for analysis and reporting. AEFI 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; the vaccination occurred between 1 January 2012 and 31 December 2013; and the residential address of the individual was recorded as NSW.

All data analyses were performed using SAS (version 9.1.3, SAS Institute, Cary, NC, USA).[23] Average annual population-based reporting rates were calculated using population estimates obtained from the Australian Bureau of Statistics.[24]

AEFI reporting rates per 100 000 administered doses were estimated where information on dose numbers was available from: the Australian Childhood Immunisation Register (ACIR) for NIP vaccines for children aged <7 years; and NSW Health data on vaccines administered in schools for 12–17 year olds. Data on adolescents does not include doses given outside the school program, which is expected to be a relatively small number.

Notes on interpretation

The data reported here are provisional only, particularly for the fourth quarter of 2013, because of reporting delays and the late onset of some reported AEFIs. Numbers are updated for previous years. The information collated in the ADRS database is intended primarily to detect signals of adverse events and to inform hypothesis generation. While AEFI reporting rates can be estimated using appropriate denominators, they cannot be interpreted as incidence rates due to under-reporting, biased reporting of suspected events, and the variable quality and completeness of information provided in individual notification reports.[12]

It is important to note that this report is based on vaccine and reaction term information collated in the Australian

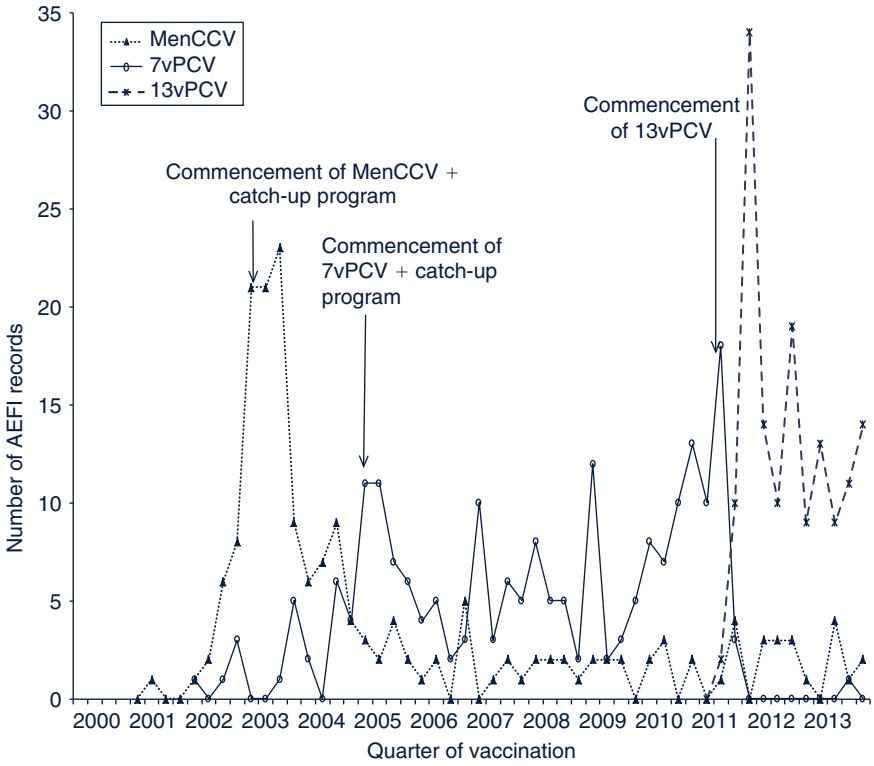

Figure 2a. Adverse events following immunisation in children aged <7 years for selected vaccines, NSW, 2000–2013, by quarter of vaccination.

NB: Meningococcal C conjugate vaccine (MenCCV) was introduced into the National Immunisation Program schedule on 1 January 2003; 7-valent pneumococcal conjugate vaccine (7vPCV) was introduced on 1 January 2005; and the 13-valent pneumococcal conjugate vaccine (13vPCV) was introduced on 1 July 2011.

Source: Adverse Drug Reactions Reporting System database, TGA.

Adverse Drug Reactions Reporting System database and not on comprehensive clinical notes.

Results

There were a total of 973 AEFI records for NSW in the ADRS database with a date of vaccination from 1 January 2012 to 31 December 2013. Of all reports, 32% ($n = 314$) were for children aged <7 years and 67% ($n = 648$) were for people aged ≥7 years. Seventy-seven per cent of AEFI ($n = 750$) were reported to the TGA via NSW Health and the remainder was reported directly to the TGA; 13% ($n = 127$) by doctors/other health care providers, 8% ($n = 78$) by members of the public, and 1% ($n = 8$) by hospitals.

Reporting trends

The overall AEFI reporting rate for 2012 and 2013 was 4.5 and 8.6 per 100 000 population respectively, compared with 6.2 in 2011.

Figure 1 shows a decline in the reported events and reporting rate per 100 000 population during 2012, which increased substantially in 2013. The vast majority of reported events (from all reporter types) were of a non-serious nature similar to previous years.[8,12] Figures 2a, 2b and 3 demonstrate marked variations in reporting levels in association with previous changes to the NIP from 2000 onwards. The increase in reports in 2013 was predominantly associated with HPV vaccines in adolescents (Figure 3).

The usual seasonal pattern of AEFI reporting from older Australians receiving 23vPPV and influenza vaccine during the autumn months (March–June) is evident in Figure 3.

Age group and vaccine

Population-based AEFI reporting rates for those ≥7 years are shown in Figure 4b. There was approximately a threefold increase in the 7 to <20 years age group during 2013 compared with 2012 (from 7.1 to 24.8; Figure 4b), associated with the introduction of HPV vaccine for boys.

Reporting rates per 100 000 doses were highest in 2 to <7 year olds during the 2012–2013 period. The rates increased substantially from 2009 onwards, and in 2013

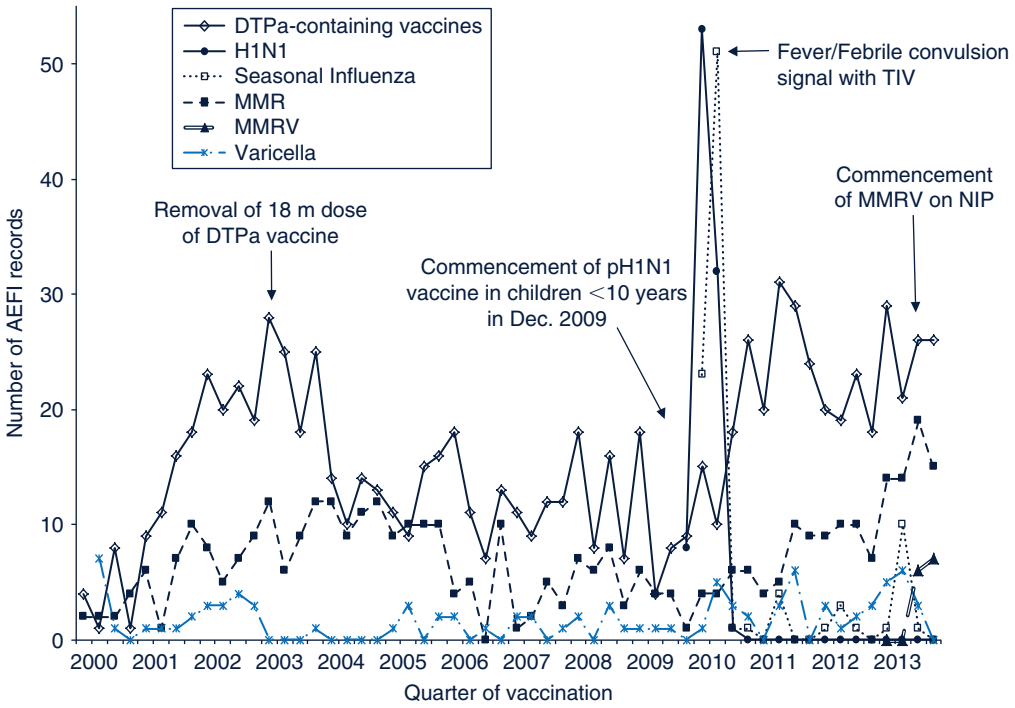

Figure 2b. Adverse events following immunisation in children aged < 7 years for selected vaccines, NSW, 2000–2013, by quarter of vaccination.

NB: DTPa-IPV was introduced into the NIP schedule in November 2005 replacing DTPa and OPV; seasonal trivalent influenza vaccine was introduced in 2010, which was an extension of existing adult and Indigenous programs to at risk populations; MMRV and HibMenC vaccines were introduced in July 2013.

Source: Adverse Drug Reactions Reporting System database, TGA.

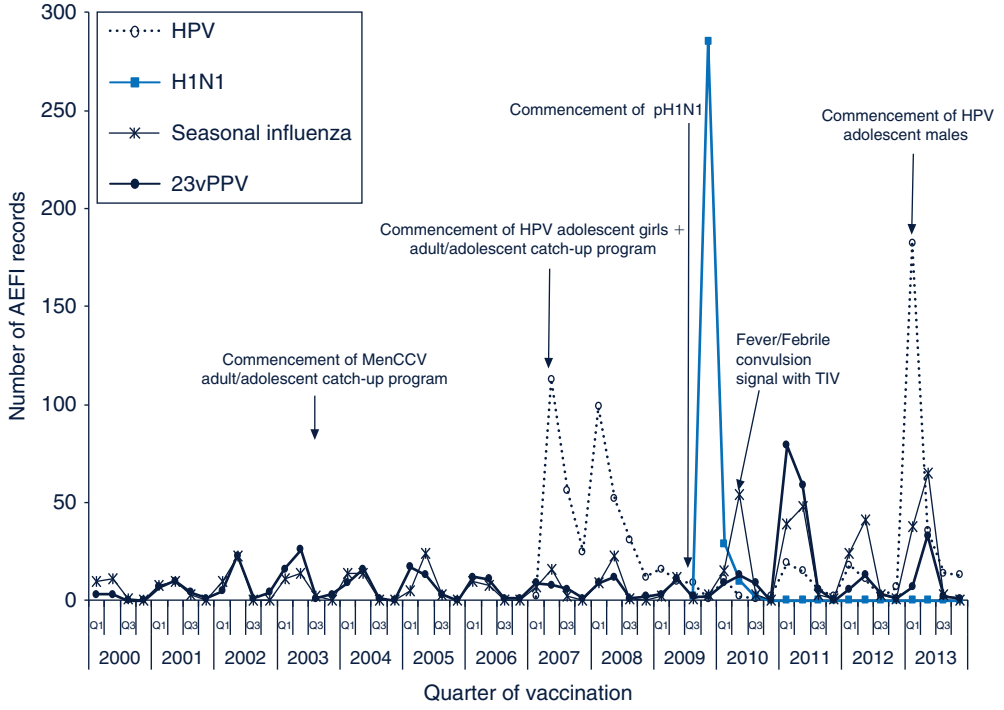

Figure 3. Adverse events following immunisation for people aged ≥7 years in frequently reported vaccines, NSW, 2000–2013, by quarter of vaccination.
Source: Adverse Drug Reactions Reporting System database, TGA.

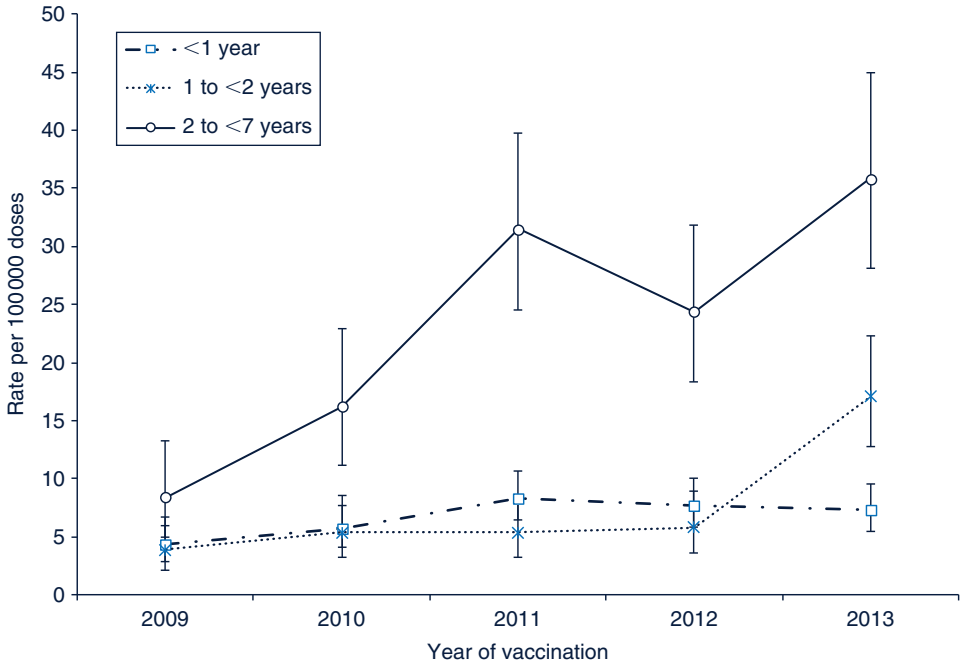

Figure 4a. Reporting rates of adverse events following immunisation for NSW per 100 000 doses, 2009–2013, for people aged <7 years, by year of vaccination.
Source: Adverse Drug Reactions Reporting System database, TGA.

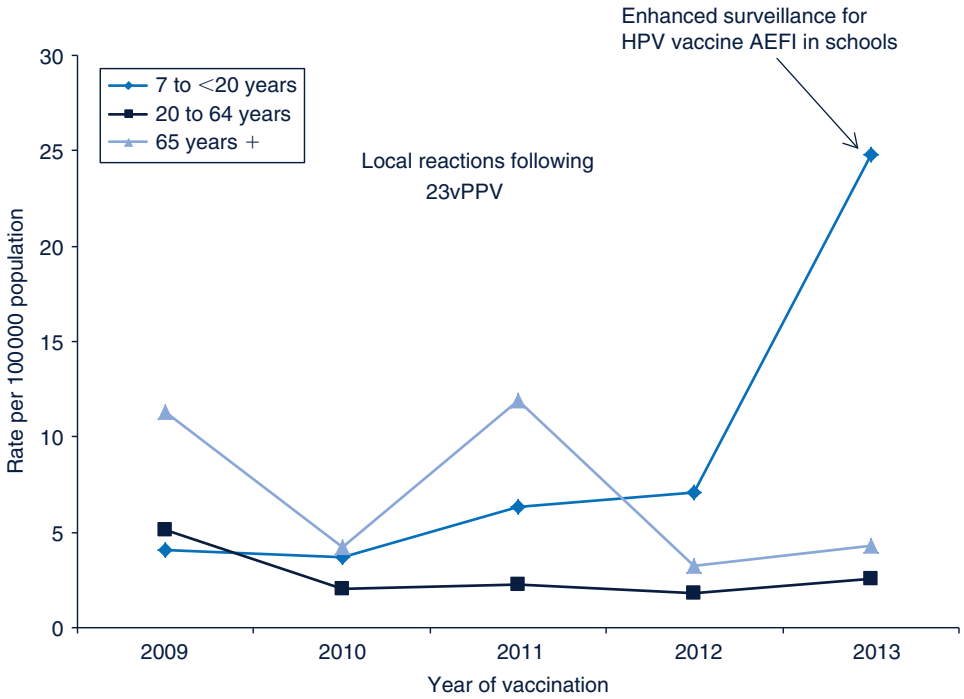

Figure 4b. Reporting rates of adverse events following immunisation for NSW per 100 000 population, 2009–2013, for people aged ≥7 years, by year of vaccination.

(35.8; 95% CI 28.1–44.9) compared with 2012 (24.4; 95% CI 18.4–31.8), but confidence intervals for those 2 years overlapped. The reasons for these changes over time are unclear, as there have been no changes in the schedule in this age group, except for the 13vPCV catch-up program in 2011 where some children in this age group received 13vPCV. The maximum increase occurred in 1 to <2 year olds associated with the introduction of MMRV in 2013, statistically significantly higher than 2012 (17.1; 95% CI 12.8–22.3 in 2013 compared with 5.8; 95% CI 3.6–8.9 in 2012 (Table 1, Figure 4a), similar to the rate in 2011 (5.4; 95% CI 3.2–8.4).

Table 1. Vaccine types listed as 'suspected' in records of adverse events following immunisation for four age groups (<7, 12–17, 18–64 and ≥65 years), NSW, 2012–2013

Vaccines[a]	AEFI records[b] (2012–2013) *n*	'Serious' outcome[c] (2012–2013) *n*	Reporting rate per 100 000 doses[d] (95% CI) 2013	Reporting rate per 100 000 doses[d] (95% CI) 2012	Reporting rate per 100 000 doses[d] (95% CI) 2011
<7 years					
Measles–mumps–rubella	102	8	34.5 (26.7–43.9)	18.5 (12.9–25.8)	13.8 (9.0–20.2)
PCV	100	6	17.6 (13.0–23.3)	16.6 (12.4–21.7)	24.2 (19.0–30.4)
DTPa-IPV	99	6	62.0 (47.1–79.8)	41.8 (29.9–57.0)	47.1 (34.3–63.0)
Hexavalent (DTPa-IPV-HepB-Hib)	85	7	16.6 (12.1–22.2)	14.7 (10.5–20.1)	21.0 (15.8–27.2)
Rotavirus	78	9	20.1 (13.9–28.0)	25.8 (18.7–34.7)	25.7 (18.6–34.7)
Varicella	23	1	26.9 (14.6–45.3)	10.2 (4.6–19.3)	10.1 (4.6–19.2)
Seasonal influenza	23	7	dna	dna	dna
MenCCV	18	1	13.9 (6.1–27.5)	9.6 (4.4–18.2)	5.3 (1.7–12.4)
HibMenC	14	1	34.4 (18.9–57.7)	n/a	n/a
Haemophilus influenzae type b	14	1	7.4 (2.0–18.8)	9.9 (4.5–18.7)	4.4 (1.2–11.2)
MMRV	13	1	30.5 (16.2–52.1)	Introduced in 2013	Introduced in 2013
12–17 years					
HPV[e]	260	12	n/a	33.6 (23.4–46.8)	37.9 (26.8–52.3)
dTpa	140	7	n/a	30.2 (21.5–41.3)	24.3 (16.4–34.7)
Hepatitis B	126	3	n/a	24.2 (16.1–35.0)	21.4 (13.8–31.9)
Varicella	24	3	n/a	20.6 (9.4–39.1)	31.2 (16.1–54.6)
Seasonal influenza	3	0	n/a	n/a	n/a
18–64 years					
Seasonal influenza	129	17	n/a	n/a	n/a
23vPPV	21	7	n/a	n/a	n/a
dTpa	21	2	n/a	n/a	n/a
Hepatitis B	17	0	n/a	n/a	n/a
Yellow fever	2	1	n/a	n/a	n/a
≥65 years					
23vPPV	40	1	24.4 (16.1–35.4)	11.7 (6.2–20.0)	97.4 (79.9–117.6)
Seasonal influenza	32	0	2.5 (1.5–4.0)	2.0 (1.1–3.3)	6.0 (4.3–8.1)
dTpa	5	0	n/a	n/a	n/a
Age group					
<1 year	109	10	7.3 (5.5–9.5)	7.7 (5.8–10.0)	8.3 (6.4–10.7)
1 to <2 years	75	6	17.1 (12.8–22.3)	5.8 (3.6–8.9)	5.4 (3.2–8.4)
2 to <7 years	130	11	35.8 (28.1–44.9)	24.4 (18.4–31.8)	31.5 (24.5–39.7)
12 to 17 years	335	16	n/a	19.1 (15.0–23.9)[f]	19.4 (15.2–24.4)[f]
18 to 64 years	197	22	n/a	n/a	n/a
65+ years	82	4	5.7 (4.2–7.5)	4.2 (2.9–5.9)	14.6 (12.1–17.4)[g]

[a]Records where at least one of the vaccines shown in the table was suspected of involvement in the reported adverse event.
[b]Number of AEFI records in which the vaccine was coded as 'suspected' of involvement in the reported adverse event and the vaccination was administered between 1 January 2012 and 31 December 2013. More than one vaccine may be coded as 'suspected' if several were administered at the same time.
[c]'Serious' outcomes are defined in the Methods section.
[d]The estimated AEFI reporting rate per 100 000 vaccine doses recorded.
[e]22 cases of HPV were for 11 year olds and 1 case 18 year old.
[f]School-based doses data only.
[g]Seasonal influenza and 23vPPV only.
AEFI: adverse events following immunisation
dna: denominator not available
n/a: not applicable
Source: Adverse Drug Reactions Reporting System database, TGA.

Table 2. Vaccine types listed as 'suspected' in records of adverse events following immunisation (AEFI), NSW, 2012–2013

Suspected vaccine type	AEFI records	One suspected vaccine or drug only[a]		'Serious' outcome		Age group[b]			
						<7 years		≥7 years	
	n	*n*	%[c]	*n*	%[c]	*n*	%[c]	*n*	%[c]
HPV	283	102	36	12	4	0	0	282	100
Influenza	192	168	88	25	13	17	9	169	88
dTpa	177	55	31	9	5	0	0	176	99
Hepatitis B	159	27	17	3	2	2	1	157	99
MMR	113	19	17	8	7	101	89	11	10
DTPa-IPV	100	41	41	6	6	99	99	1	1
PCV	99	11	11	6	6	99	100	0	0
DTPa-IPV-HepB-Hib	86	3	3	7	8	85	99	1	1
Rotavirus	78	14	18	9	12	78	100	0	0
23vPPV	67	50	75	8	12	1	1	62	93
Varicella	49	24	49	4	8	23	47	26	53
MenCCV	21	4	19	1	5	17	81	3	14
HibMenC	14	2	14	1	7	14	100	0	0
Hib	14	0	0	1	7	14	100	0	0
MMRV	13	12	92	1	8	13	100	0	0
Hepatitis A	7	2	29	2	29	1	14	6	86
Typhoid	7	1	14	1	14	0	0	7	100
Hepatitis A-Typhoid	6	4	67	0	0	0	0	6	100
Q fever	4	4	100	0	0	0	0	4	100
Yellow fever	4	4	100	1	25	0	0	4	100
dT	4	3	75	0	0	0	0	4	100
dTpa-IPV	3	1	33	0	0	0	0	3	100
Hepatitis A + B	2	1	50	0	0	0	0	2	100
Polio	2	1	50	0	0	0	0	2	100
Cholera	1	1	100	0	0	0	0	1	100
Tetanus	1	1	100	1	100	0	0	1	100
Total[d]	973	558	57	70	7	314	32	648	67

[a]AEFI records where only one vaccine was suspected of involvement in a reported adverse event.
[b]AEFI records are not shown if both age and date of birth were not reported.
[c]Percentages are calculated for the number of AEFI records where the vaccine was suspected of involvement in the AEFI, e.g. HPV was 'suspected' in 283 AEFI records; this was the only suspected vaccine in 36% of the 283 AEFI records, 4% were defined as 'serious' and 100% were for those aged ≥7 years.
[d]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 one vaccine.
Source: Adverse Drug Reactions Reporting System database, TGA.

Reporting rates per 100 000 doses in <7 year olds, which exclude influenza due to the absence of reliable dose data, did not change significantly for any vaccine (Table 1). In 2013 there was a statistically significant increase in MMR rates compared with 2012 (Table 1).

The most frequently reported individual vaccine during 2012–2013 was HPV ($n = 283$; 29% in 2012–2013 compared with $n = 42$ (9%) in 2011), followed by seasonal influenza vaccine ($n = 192$; 20% in 2012–2013 compared with $n = 93$ (21%) in 2011), dTpa ($n = 177$; 18% in 2012–2013 compared with $n = 62$ (14%) in 2011), MMR ($n = 113$; 12% in 2012–2013 compared with $n = 29$ (6%) in 2011) and DTPa-IPV ($n = 100$; 10% in 2012–2013 compared with $n = 45$ (10%) in 2011) (Table 2).

Reactions

The distribution and frequency of reactions listed in AEFI records for 2012–2013 are shown in Table 3. The most frequently reported adverse events were injection site reaction (ISR) ($n = 230$; 24%), syncope ($n = 181$; 19%), and pyrexia and rash ($n = 113$; 12% each) (Table 3).

Of the total 230 cases of ISR, 81 (35%) were children aged <7 years and 145 (63%) were aged ≥7 years. The most

Table 3. Outcomes of adverse events following immunisation[a] for two age groups (<7 and ≥7 years), NSW, 2012–2013

Outcome	AEFI records *n* (%)[b]	Age group	
		<7 years *n* (%)[c]	≥7 years *n* (%)[c]
Non-serious	795 (82)	249 (31)	537 (68)
Unknown[d]	108 (11)	38 (35)	68 (63)
Serious:	70 (7)	27 (39)	43 (61)
recovered with sequelae	0 (0)	0 (0)	0 (0)
hospital treatment – admission	59	25 (42)	34 (58)
life-threatening event	9	1 (11)	8 (89)
death	2	1 (50)	1 (50)
Total	973 (100)	314 (32)	648 (67)

[a]Causal connection between vaccination and adverse event not necessarily established.
[b]Percentages relate to the total number of AEFI records ($n = 973$).
[c]Percentages relate to the number of AEFI records with the specific outcome (e.g. of 795 AEFI records with a 'non-serious' outcome, 31% were for children aged under 7 years).
[d]'Unknown' outcome relates to the number of AEFI records that are not serious and with unknown outcome.
AEFI: adverse events following immunisation
Source: Adverse Drug Reactions Reporting System database, TGA.

commonly suspected vaccines for <7 year olds related to ISR were DTPa-IPV ($n = 52$), MMR ($n = 32$) and PCV ($n = 14$), while for ≥7 year olds these were seasonal influenza vaccine ($n = 49$; 38 in the 18–64 years age group and 8 in ≥65 year olds), dTpa ($n = 35$; 21 reports in the 12–17 years age group), 23vPPV ($n = 42$; 14 in the 18–64 years age group and 27 in ≥65 year olds) and HPV ($n = 21$; 20 in the 12–17 years age group), either given alone or co-administered with other vaccines.

There were 181 reported cases of syncope during the 2012–2013 period. Six cases were reported in <7 year olds: three following co-administration of DTPa-IPV and MMR vaccine; one following co-administration of hexavalent DTPa-IPV-HepB-Hib, rotavirus and pneumococcal conjugate vaccines; and one each following hepatitis B and influenza vaccine administered alone. One hundred and seventy-five cases were reported in ≥7 year olds. The majority were following receipt of HPV ($n = 149$), HepB ($n = 76$) and dTpa ($n = 62$), either given alone or co-administered with other vaccines.

There were 12 reports of hypotonic-hyporesponsive episode (HHE); 11 reported from children aged <7 years. Of the 11 reported cases in <7 year olds, five were following co-administration of hexavalent/pneumococcal conjugated vaccine/rotavirus vaccines and two were following co-administration of DTPA-IPV/MMR.

Severity of outcomes

Seven percent ($n = 70$; 7%) of events were defined as 'serious' (i.e. recovery with sequelae, requiring hospitalisation, experiencing a life-threatening event or death), which is lower than what was observed in 2011 ($n = 44$; 10%). Numbers of reported events and events with outcomes defined as 'serious' are shown in Table 4.

The reactions recorded as 'serious' were ISR ($n = 11$), convulsions ($n = 11$) including four febrile convulsions, pyrexia ($n = 8$), syncope ($n = 6$), diarrhoea and vomiting ($n = 3$ each), presyncope ($n = 4$), three cases each of anaphylaxis, intussusception and HHE, one case of Guillain-Barrè syndrome (GBS) and two reported deaths.

There were five cases of anaphylaxis; one occurred 10 min post administration of seasonal influenza vaccine, the second one was 5–10 min post vaccination with 23vPPV and seasonal influenza vaccine, the third one was following seasonal influenza vaccine, time not specified, the fourth one was following co-administration of DTPa-IPV and MMR vaccine and the last one was following vaccination with hexavalent/pneumococcal conjugated vaccine/rotavirus vaccines given concomitantly.

The only reported case of GBS was in a person aged >60 years following co-administered seasonal influenza and 23vPPV vaccines. The person experienced coryzal symptoms for 4 days after receiving the vaccines and developed symptoms of GBS approximately 11 days post vaccination.

There were two deaths reported as temporally associated with receipt of vaccines.

- A 28-year-old person, who became unwell 2–3 days post vaccination with an unspecified influenza vaccine. The person developed thrombotic thrombocytopenic purpura (TTP) and died 2 days after onset of symptoms. The cause of the death was documented as TTP.

Table 4. Selected reported adverse events and reactions of interest[a] as classified predominantly by MedDRA Preferred Terms in records of adverse events following immunisation (AEFI), NSW, 2012–2013[b]

MedDRA Preferred Terms (adverse events)	AEFI records	Only reaction reported[c]		'Serious' outcome		Age group[d]			
						<7 years		≥7 years	
	n	*n*	%[e]	*n*	%[e]	*n*	%[e]	*n*	%[e]
Injection site reaction[f]	230	100	43	11	5	81	35	145	63
Syncope	181	152	84	6	3	6	3	175	97
Rash[g]	113	43	38	4	4	71	63	42	37
Pyrexia	113	2	2	8	7	54	48	54	48
Vomiting	69	5	7	3	4	32	46	36	52
Headache	65	4	6	4	6	3	5	60	92
Extensive limb swelling	56	23	41	1	2	29	52	27	48
Nausea	52	0	0	2	4	2	4	50	96
Urticaria	45	17	38	3	7	21	47	23	51
Dizziness	40	1	3	0	0	0	0	40	100
Lethargy	39	1	3	3	8	11	28	26	67
Malaise	38	2	5	2	5	2	5	35	92
Convulsions[h]	35	22	63	11	31	28	80	7	20
Presyncope	33	23	70	4	12	1	3	32	97
Arthralgia	33	4	12	2	6	0	0	31	94
Diarrhoea	30	0	0	3	10	18	60	12	40
Paraesthesia	26	2	8	2	8	0	0	31	94
Myalgia	24	1	4	0	0	0	0	22	92
Influenza-like illness	23	5	22	0	0	0	0	21	91
Pruritus	23	4	17	1	4	6	26	17	74
Pallor	16	0	0	1	6	9	56	7	44
Abdominal pain	15	1	7	1	7	4	27	11	73
Hypersensitivity	15	7	47	2	13	3	20	12	80
Dyspnoea	14	0	0	2	14	2	14	11	79
Erythema	12	3	25	0	0	9	75	3	25
Cough	12	0	0	0	0	6	50	6	50
Chills	12	0	0	1	8	1	8	11	92
Hypotonic-hyporesponsive episodes	12	9	75	3	25	11	92	1	8
Decreased appetite	12	0	0	2	17	5	42	7	58
Pain in extremity	11	1	9	1	9	0	0	11	100
Chest discomfort	10	1	10	0	0	0	0	10	100
Abdominal pain upper	9	0	0	1	11	0	0	9	100
Tremor	9	1	11	0	0	1	11	8	89
Rhinorrhoea	9	0	0	0	0	7	78	2	22
Swelling face	9	1	11	3	33	4	44	5	56
Irritability	9	0	0	1	11	9	100	0	0
Screaming	9	0	0	1	11	9	100	0	0
Fatigue	8	0	0	0	0	0	0	7	88
Crying	8	2	25	1	13	8	100	0	0
Lymphadenopathy	7	0	0	1	14	1	14	6	86
Oropharyngeal pain	7	0	0	0	0	0	0	7	100
Anaphylactic reaction	5	3	60	3	60	2	40	3	60
Pain	5	0	0	1	20	1	20	3	60
Somnolence	5	0	0	0	0	2	40	3	60
Hyperhidrosis	4	0	0	0	0	1	25	2	50
Intussception	3	3	100	3	100	3	100	0	0
Encephalitis	1	0	0	1	100	0	0	1	100
Guillain-Barre syndrome	1	0	0	1	100	0	0	1	100

[a]Selected reported adverse events reported during January 2012–December 2013. Note: for injection site reaction, rash and convulsions, preferred terms were grouped as described below.
[b]A complete list of adverse reactions as classified by individual preferred terms is available on request.
[c]AEFI records where only one reaction was reported.
[d]Not shown if neither age nor date of birth were recorded or missing data.
[e]Percentages relate to the number of AEFI records in which the specific reaction term was listed, e.g. of 230 AEFI records listing injection site reaction, 43% listed only one type of reaction and 35% were for children aged <7 years.
[f]Injection site reaction MedDRA codes include 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.
[g]Rash MedDRA codes include rash, rash generalised, rash maculo-papular, rash macular, rash vesicular, rash papular, rash morbilliform, and rash pustular.
[h]Convulsion MedDRA codes include febrile convulsion, and convulsion, grand mal convulsion, and partial seizures.
Source: Adverse Drug Reactions Reporting System database, TGA.

- A 1-year-old child who had received Hib, MenC and MMR vaccines 5 days prior to death.

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

New National Immunisation Program vaccines

Human papillomavirus vaccine

A total of 283 AEFI reports were received for HPV vaccine in 2013 compared with 38 in 2012. Of these, 12 cases were coded as serious. Forty-five percent of cases were reported in males and 55% in females. HPV was the only suspected vaccine in 102 records (36%) (Table 2). Ninety-four per cent of AEFI ($n = 266$) were reported to the TGA via NSW Health and the remainder was reported directly to the TGA: 3% ($n = 9$) by doctors/other health care providers; 0.4% ($n = 1$) by hospitals; and 2% ($n = 7$) by members of the public).

The most commonly reported AEFI was syncope ($n = 150$; 53%), followed by headache ($n = 25$; 9%), nausea ($n = 22$; 8%), dizziness, rash and injection site reactions (7% each), pre-syncope ($n = 18$; 6%), pyrexia ($n = 15$; 5%) and urticaria ($n = 9$; 3%).

MMRV vaccine

There was a total of 13 AEFI records for 2013 where MMRV vaccine was recorded (Table 4). Of these, one was coded as serious. The reporting rates for <7 year olds were 30.5 per 100 000 doses (Table 1). In ninety-two percent of the reports MMRV ($n = 12$) was administered alone.

The spectrum of reactions for MMRV included 9 (69%) reports of rash, 4 (31%) of pyrexia, 3 cases (23%) of convulsions including 2 febrile convulsions, and 2 cases of injection site reactions (15%).

Discussion

This report uses a different methodology of analysis than that used in previous annual reports for specific AEFIs. The methodological framework used here allows for a clearer reporting of adverse events using MedDRA PTs. This change in methodology needs to be taken into account when comparing with data from previous annual reports on specific reaction terms and categories.

There was an overall drop in the number of reports and population-based rates in 2012 compared with 2011, predominantly due to a large decline in reports following vaccination with 23vPPV vaccine. However, in 2013, both numbers and rates increased. This was predominantly due to a larger adolescent vaccine target group, and the use of enhanced safety surveillance, implemented as part of the extension of the National HPV Vaccination Program to males aged 12–13 years with a catch-up program for males aged 14–15 years.

The TGA, together with NSW Health, closely monitored adverse events reported following HPV vaccination as the program was extended to males, particularly enhanced surveillance using rapid reporting from school-based programs. This aimed to detect four conditions: (1) anaphylaxis; (2) generalised allergic reactions; (3) loss of consciousness (simple faints [syncope], faints with injury, faints with convulsion); and (4) any condition requiring emergency department attendance or hospitalisation. In addition, historical data show 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 they are not familiar with, followed by a reduction and stabilisation of reporting over time (Weber effect).[25] This enhanced propensity to report events following newer vaccines increases the sensitivity of the system to detect signals of serious, rare or previously unknown events.

The majority of the AEFI reports for HPV vaccine were mild and had been identified in pre-registration clinical trials.[26] These included injection site reactions, syncope, mild allergic reactions, and a range of mild non-specific symptoms including headache, nausea, dizziness, malaise and weakness. A similar range of events has previously been reported to the TGA associated with the HPV program for girls.[4,27,28] The enhanced surveillance implemented in schools in February 2013 resulted in increased reporting of syncope following HPV vaccine. Syncope, usually due to a vasovagal response to having an injection, is recognised as a potential AEFI following any immunisation, with highest reporting rates for syncope in adolescents.[29,30]

The increase in reports for children aged 1 to <2 years in 2013 was primarily due to vaccination with MMR, MMRV and HibMenC vaccines either administered alone or together; two of these were new vaccines on the NIP in 2013 and as such this increased rate of reporting is not unexpected. In addition, active surveillance for febrile seizures following measles-containing vaccines was implemented in paediatric hospitals (in the Paediatric Active Enhanced Disease Surveillance [PAEDS] network)[31] as part of enhanced surveillance for the introduction of MMRV to the NIP.

Conclusion

Overall, the total number of reported AEFI increased during the 2012–2013 reporting period compared with 2011, a continuation of recent trends in increasing propensity to report and consequent to the introduction of several new vaccines/groups newly eligible for existing vaccines.

The majority of AEFIs reported to the TGA were mild transient events.

The higher reporting rates are also related to numerous activities undertaken by the TGA and NSW Health to encourage and facilitate reporting of AEFI. The data reported here are consistent with an overall high level of safety for vaccines included in the NIP schedule.

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