Surveillance of adverse events following immunisation, NSW, 2019

***Catherine Glover*[A,D], *Aditi Dey*[A], *Han Wang*[A], *Helen Quinn*[A], *Paola Garcia*[B], *Megan Hickie*[C], *Frank Beard*[A] *and Kristine Macartney*[A]**

[A]*National Centre for Immunisation Research and Surveillance, The Children's Hospital at Westmead.*

[B]*Health Protection NSW.*

[C]*Pharmacovigilance and Special Access Branch, Therapeutic Goods Administration.*

[D]*Corresponding author. Email: catherine.glover1@health.nsw.gov.au*

Abstract: Aim: This report summarises spontaneous surveillance data for adverse events following immunisation (AEFI) in New South Wales (NSW) from 1 January 2019 to 31 December 2019. **Methods:** Analysis of de-identified data on all AEFI reported to the Therapeutic Goods Administration (TGA) for individuals from NSW. An AEFI is defined as any untoward medical occurrence which follows immunisation; AEFI may be coincidental or may be caused by a vaccine(s), or during handling or administration. **Results:** There were 666 AEFI reported for vaccines administered from 1 January to 31 December 2019. Of all AEFI, 4% were reported in Aboriginal and Torres Strait Islander people. There was a statistically significant decrease in the overall AEFI reporting rate (8.2 per 100 000 population, 95% CI 7.6–8.9 per 100 000 population) in 2019 compared with 2018 (10.6 per 100 000 population, 95% confidence interval 9.9–11.3 per 100 000 population). Approximately 14% of AEFI were classified as serious in 2019, a decrease over 2018 (24%). The vast majority of reported events were of a non-serious nature, similar to those in previous years. Overall, the most commonly reported adverse events were associated with the following vaccines: seasonal influenza (34.8%), 13vPCV (12.3%), DTPa-IPV-HepB-Hib (11.7%), DTPa-IPV (10.5%), dTpa (10.1%), MMR (8.9%), rotavirus (8.4%), HPV (7.8%) and meningococcal ACWY (7.5%). The most frequently reported adverse events were injection site reaction (177), rash (137), pyrexia (116), vomiting (57), urticaria (55), pain (43), headache (43) and nausea (32). There was one death reported in this period. **Conclusion:** There was a decrease in the reporting rate for AEFI from NSW in 2019 compared with 2018. The majority of AEFI reported to the TGA were mild transient events. These data are useful to inform the ongoing immunisation programs in NSW.

Abbreviations of vaccine types

BCG	Bacille Calmette-Guérin
DTPa	diphtheria-tetanus-pertussis (acellular) – paediatric formulation
dTpa	diphtheria-tetanus-pertussis (acellular) – adolescent and adult formulation
dTpa-IPV	combined dTpa and inactivated poliovirus
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)
Hib	*Haemophilus influenzae* type b
Hib-MenC	combined *Haemophilus influenzae* type b and meningococcal C vaccine
HPV	human papillomavirus
IPV	inactivated poliovirus vaccine
MenACWY	quadrivalent meningococcal (serogroups A, C, W-135, Y) conjugate vaccine
MenB	meningococcal B
MenCCV	meningococcal C conjugate vaccine
MMR	measles-mumps-rubella
MMRV	measles-mumps-rubella-varicella
pH1N1	pandemic influenza A (H1N1)
7vPCV	7-valent pneumococcal conjugate vaccine
13vPCV	13-valent pneumococcal conjugate vaccine
23vPPV	23-valent pneumococcal polysaccharide vaccine

Introduction

This is the 11th in a series of annual reports of adverse events following immunisation (AEFI) in New South Wales (NSW). This report summarises spontaneous AEFI

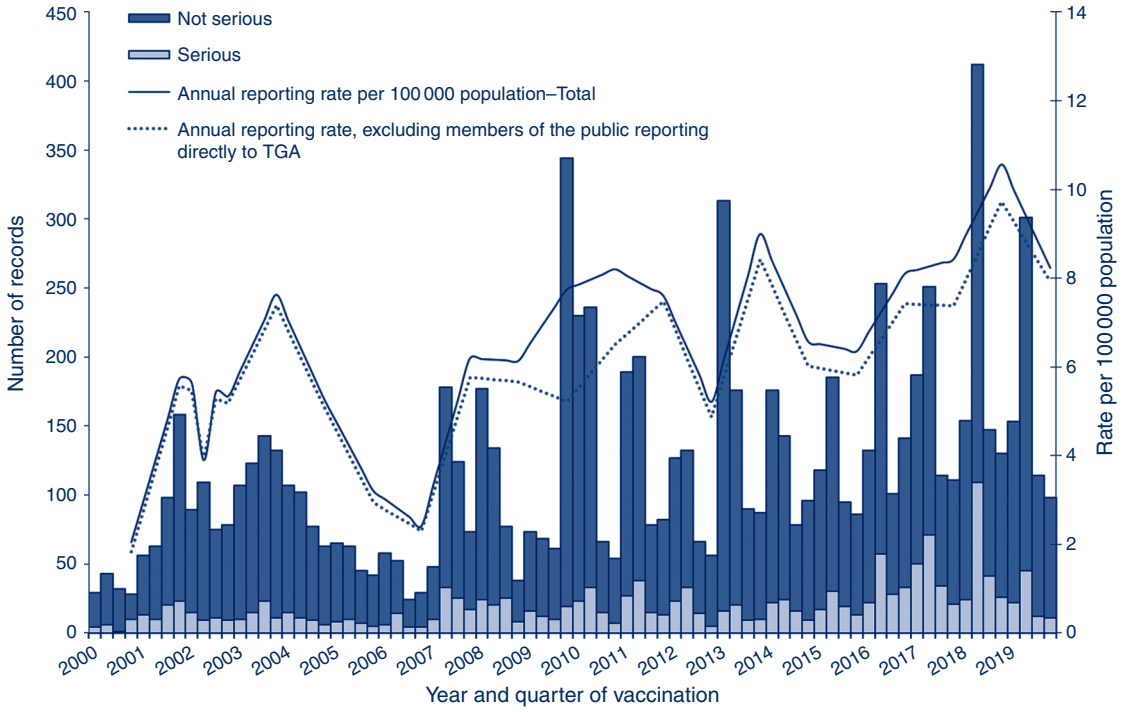

Figure 1. Reports of adverse events following immunisation, NSW, 2000–2019, by quarter of vaccination.

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 Events Management System database, Therapeutic Goods Administration.

surveillance data reported from NSW for 2019 and describes reporting trends over the 20-year period 2000–2019.

An adverse event following immunisation is defined as any untoward medical occurrence which 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 surveillance of AEFI after the Therapeutic Good Administration (TGA) approves a vaccine is particularly important to detect rare, late onset and unexpected events, and new vaccine safety signals which are difficult to detect in pre-licensure vaccine trials.

Trends in reported AEFI are heavily influenced by changes to the schedule of vaccines provided through the National Immunisation Program (NIP). Changes to the NIP in previous years have been reported elsewhere.[2–12] Recent NIP and NSW immunisation schedule changes that may have affected AEFI surveillance data in NSW presented in this report are:

- April 2019
  - Annual seasonal influenza vaccination NIP-funded for Aboriginal and Torres Strait Islander children and adolescents aged 5–14 years.
  - Meningococcal ACWY vaccine NIP-funded for adolescents aged 14–16 years in a school-based vaccination program, as well as adolescents aged 15–19 years through primary care providers. Previously funded for adolescents by NSW from May 2017 to March 2019.

Methods

AEFI are notifiable to NSW public health units by medical practitioners and hospital chief executive officers under the *Public Health Act 2010* (NSW). Cases with any missing information and all serious AEFI are followed up by public health units and Health Protection NSW. All notifications are forwarded to the TGA. The TGA also receives reports directly from vaccine manufacturers, members of the public and other sources. The TGA sends these reports to NSW Health, and they are included in this report.[13,14]

Adverse events following immunisation data

Notifications from all sources across Australia are received by the TGA, coded using internationally consistent criteria[15] and entered into the TGA's Adverse Events Management System (AEMS). The term 'AEFI record' is used throughout this report to signify the occurrence of an AEFI because a single adverse event can result in more than one notification and generate more than one record in the AEMS. Duplication of adverse event reports/cases is more likely to occur in situations where there are sequential adverse events in a single patient or if multiple vaccines are involved. Records identified as duplicates are linked and not included as separate reports.

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

Study definitions of AEFI outcomes

Australian sponsors are required to apply seriousness coding to AEFI reports to ensure legislated requirements are met. Reports are coded by the TGA as 'serious' or 'non-serious' based on criteria similar to those used by the World Health Organization[16] and the United States Vaccine Adverse Events Reporting System (VAERS).[17]

In this report, an adverse event is defined as 'serious' if it meets one or more of the following criteria:

- results in death;
- is life-threatening;
- requires inpatient hospitalisation or prolongation of existing hospitalisation;
- results in persistent or significant disability/incapacity;
- is a congenital anomaly/birth defect;
- is a medically important event or reaction.

Data analysis

De-identified information on AEFI reports from the TGA's AEMS database was released to NCIRS in March 2020. AEFI records contained in the AEMS 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 2000 and 31 December 2019 (or if vaccination date was missing, the date of onset of symptoms or signs occurred between 1 January 2000 and 31 December 2019);
- the residential address of the individual was recorded as within NSW.

Vaccines are classified as 'suspected' if the notification/report contains sufficient information to be valid and a causal relationship between reported adverse events and the vaccine is deemed at least possible.

Data cleaning was performed using SAS (version 9.4, SAS Institute, Cary, NC, USA).[18] Data analyses were conducted using Stata (version 14.2, StataCorp, College Station, TX, USA) and R (version 3.6.0, R Foundation for Statistical Computing, Vienna, Austria).[19,20] Average annual population-based reporting rates were calculated

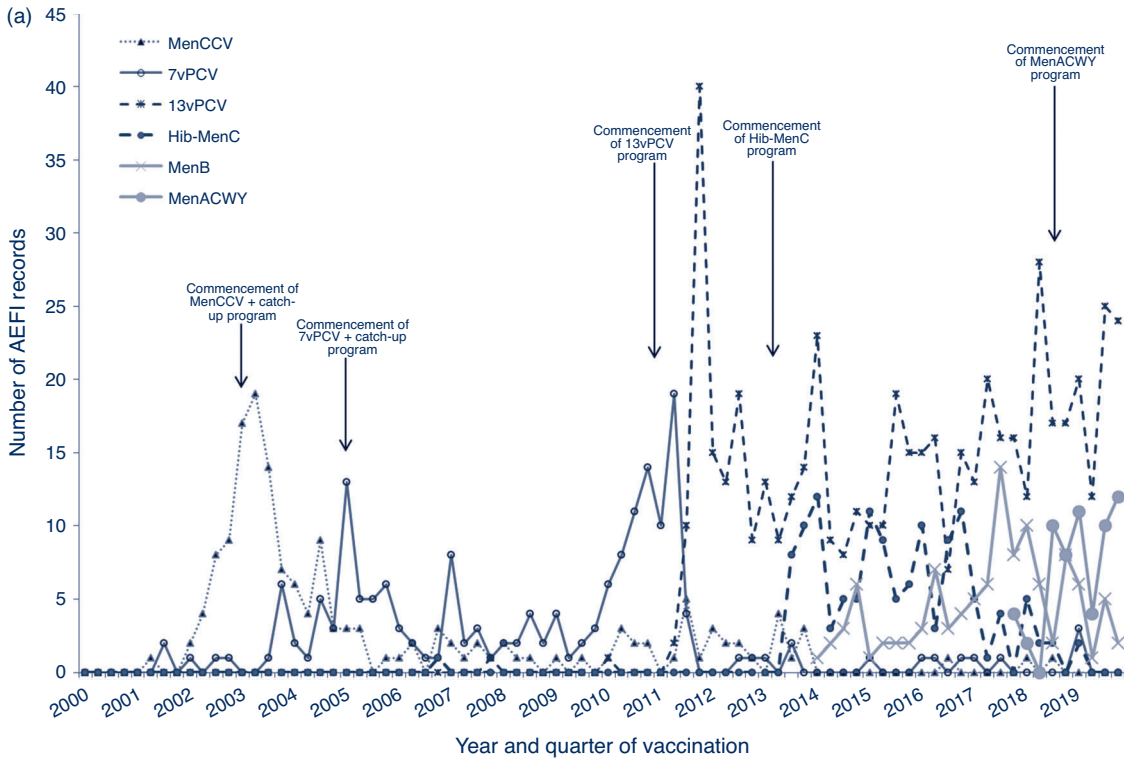

Figure 2a. Adverse events following immunisation in children aged <7 years for selected vaccines, NSW, 2019, by quarter of vaccination.

NB: Meningococcal C conjugate vaccine (MenCCV) was introduced into the National Immunisation Program schedule on 1 January 2003; 7-valent pneumococcal conjugate vaccine (7vPCV) on 1 January 2005; 13-valent pneumococcal conjugate vaccine (13vPCV) on 1 July 2011; and Hib–MenC on 1 July 2013 and MenACWY vaccine was introduced at 12 months in July 2018.

Source: Adverse Events Management System database, Therapeutic Goods Administration.

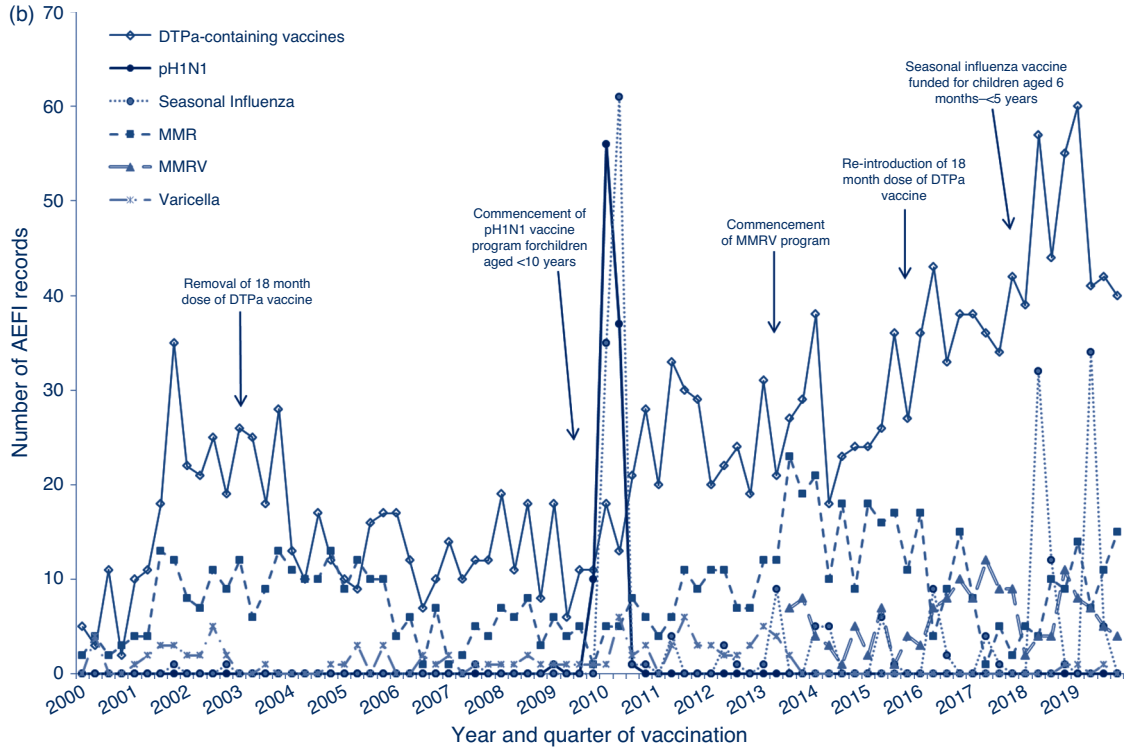

Figure 2b. Adverse events following immunisation in children aged <7 years for selected vaccines, NSW, 2000–2019, by quarter of vaccination.

NB: DTPa-IPV was introduced into the NIP schedule in November 2005 replacing DTPa and oral polio vaccine (OPV); commencement of the pH1N1 (pandemic influenza vaccine) in children aged <10 years occurred in December 2009; seasonal trivalent influenza vaccine was extended to medically at risk children in 2010; seasonal quadrivalent influenza vaccine was state-funded from 2018 for children aged 6 months to <5 years, and enhanced immunogenicity trivalent influenza vaccine for individuals aged ≥65 years was introduced in 2018; MMRV vaccine was introduced on 1 July 2013 and re-introduction of 18-month booster dose of DTPa vaccine occurred in April 2016.

Source: Adverse Events Management System database, Therapeutic Goods Administration.

using mid-year population estimates obtained from the Australian Bureau of Statistics.[21] Vaccine dose counts were calculated using data from the Australian Immunisation Register (AIR) as on 31 March 2020 for doses recorded from 1 January 2019 to 31 December 2019. AEFI reporting rates per 100 000 vaccine doses recorded were estimated. Although AIR records vaccinations given to people of all ages in Australia, data for adolescent and adult vaccinations are less complete than for childhood immunisations.[22] Exact Poisson 95% confidence intervals (CI) were calculated for reporting rates per 100 000 population and per 100 000 vaccine doses.

Notes on interpretation

The data reported here are provisional only, particularly for the fourth quarter of 2019, because of reporting delays and the late onset of some reported AEFI. Numbers have been updated for previous years.

It is important to note that this report is based on vaccine and adverse event information collated in the AEMS database and not on comprehensive clinical notes. Also, Indigenous status is not routinely recorded in all AEFI reports received by the TGA and so is likely to be underestimated.

Results

There were a total of 666 AEFI records in the AEMS database with a date of vaccination during 2019 and where the vaccinated person was a resident in NSW. Of these, 58% were females (389), 40% (268) were males and 1% (9) had their gender information missing in the database. Also, 4% (29) were reported as Aboriginal and Torres Strait Islander people. Of all 666 reports, 43% (289) were for children aged <7 years and 55% (366) were for people aged ≥7 years. Approximately 2% (11) had age missing in the database. Fifty-two per cent (348) of AEFI records were reported by the state health department (i.e. via public health units to NSW Health), 42% (279) were reported by health professionals, 4% (25) by patients/consumers and 2% (14) by pharmaceutical companies.

Reporting trends

The overall AEFI reporting rate for 2019 was 8.2 per 100 000 population (95% CI 7.6–8.9 per 100 000

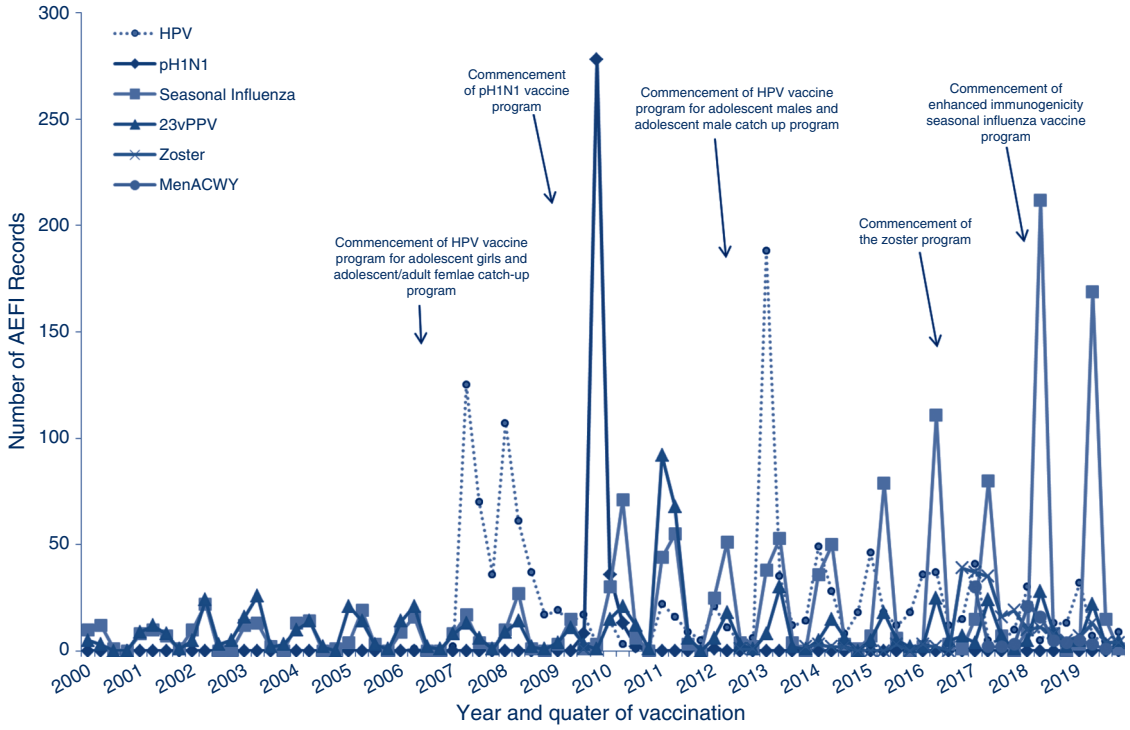

Figure 3. Adverse events following immunisation for people aged ≥7 years in frequently reported vaccines, NSW, 2000–2019, by quarter of vaccination.

NB: 4vHPV vaccine was NIP funded for females aged 12–13 years with a catch up program for females aged 14–26 years in mid-2007; commencement of the pH1N1 (pandemic influenza vaccine) in children and adults occurred in December 2009; 4vHPV was NIP funded for males aged 12–13 years with a catch up program for males aged 14–15 years in February 2013; zoster vaccine was NIP funded for people aged 70 years with a catch up program for people aged 71–79 years and enhanced immunogenicity trivalent seasonal influenza vaccines were NIP funded for people aged ≥65 years in April 2018.

Source: Adverse Events Management System database, Therapeutic Goods Administration.

population), a statistically significant decrease compared with 10.6 per 100 000 in 2018 (95% CI 9.9–11.3 per 100 000 population) (Fig. 1). The vast majority of reported events (86%) in 2019 were of a non-serious nature, similar to those in previous years.[8,12,23,24]

Figures 2a, 2b and 3 demonstrate variations in reporting for select vaccines in people aged <7 or ≥7 years, in association with changes to the NIP from 2000 onwards.

The usual seasonal pattern of AEFI reporting in older Australians receiving 23-valent pneumococcal polysaccharide vaccine (23vPPV) and influenza vaccine during the autumn to winter months (March–June) is evident in Figure 3. This seasonal pattern is also apparent in Figure 2b for children aged <7 years, especially from commencement of state-based funding for seasonal influenza vaccine in children aged 6 months to <5 years in 2018.

Age group and vaccine

Figure 4a shows that among children aged <7 years, the estimated AEFI reporting rate was highest in children aged 2 to <7 years during 2019 (36.9 per 100 000 doses, 95% CI 30.4–44.4 per 100 000 doses), a decrease over 2018 (48.2 per 100 000 doses, 95% CI 40.5–57.0 per 100 000 doses), although not statistically significant. Also, no statistically significant changes were observed in reporting rates for children aged <2 years in 2019 compared with 2018, although the reporting rates appeared to decrease.

Although vaccine dose information was available from AIR for people aged ≥7 years from 30 September 2016 onwards, the data completeness was variable across age groups. Therefore, we only estimated population-based AEFI reporting rates in these age groups (Fig. 4b). There was a statistically significant 5.2 percentage point decrease in estimated AEFI reporting rates in the ≥65 years age group in 2019 (6.4 per 100 000 population, 95% CI 5.2–8.0 per 100 000 population) compared with 2018 (11.7 per 100 000 population, 95% CI 9.9–13.7 per 100 000 population). Although there was a 3.1 percentage point decrease in estimated AEFI reporting rates in the 7 to <20 years age group during 2019 (7.9 per 100 000 population, 95% CI 6.5–9.7 per 100 000 population) compared with 2018 (11.1 per 100 000 population, 95% CI 9.3–13.1 per 100 000 population), this was not statistically significant. For those aged between 20 and <65 years, the estimated AEFI reporting rate was similar

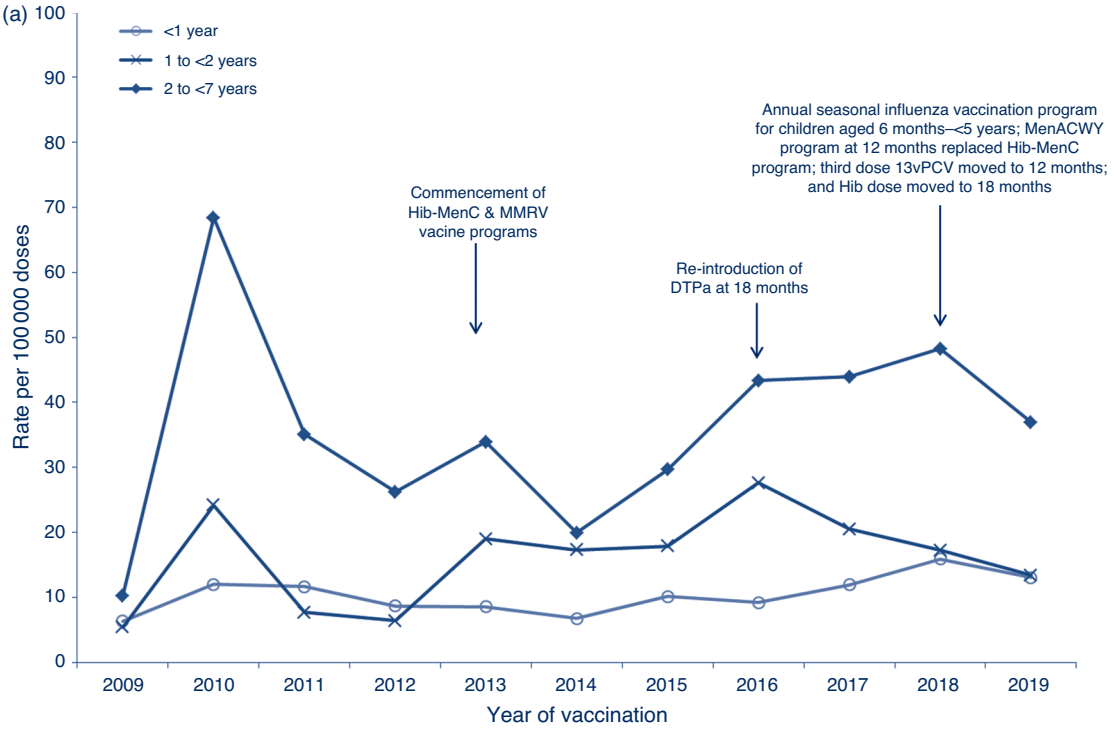

Figure 4a. Reporting rates of adverse events following immunisation for NSW per 100 000 doses, 2009–2019, for children aged <7 years, by year of vaccination.

NB: Hib-MenC was NIP funded for infants aged 12 months, and MMRV was NIP funded for children aged 18 months, in July 2013; DTPa was re-introduced to the NIP schedule for children aged 18 months in March 2016; seasonal influenza vaccine was state funded for children aged 6 months to <5 years in April 2018; and MenACWY replaced Hib-MenC at 12 months, the third dose of 13vPCV was moved from 6 months to 12 months, and a monovalent Hib dose was introduced at 18 months on the NIP schedule in July 2018.

Source: Adverse Events Management System database, Therapeutic Goods Administration.

for 2019 (3.8 per 100 000 population) compared with 2018 (4.0 per 100 000 population).

Among children aged <7 years, 13-valent pneumococcal conjugate vaccine (13vPCV) was associated with the most AEFI records (81 reports) (Table 1). For those aged between 12 and 17 years, there were 46 reports related to human papillomavirus (HPV) vaccine. In those aged ≥65 years, seasonal influenza vaccine was recorded in 44 reports. Overall, as shown in Table 2, reported adverse events were associated most commonly with seasonal influenza (34.8%), 13vPCV (12.3%), combined diphtheria-tetanus-pertussis (acellular), inactivated poliovirus, hepatitis B and Haemophilus influenzae type b (DTPa-IPV-HepB-Hib; 11.7%), combined diphtheria-tetanus-pertussis (acellular) and inactivated poliovirus (DTPa-IPV; 10.5%), diphtheria-tetanus-pertussis (acellular) – adolescent and adult formulation (dTpa; 10.1%), measles-mumps-rubella (MMR; 8.9%), rotavirus (8.4%), HPV (7.8%) and meningococcal ACWY (7.5%) vaccines.

Adverse events in 2019

The distribution and frequency of adverse events listed in AEFI records for 2019 are shown in Table 3. The most frequently reported adverse events were injection site reaction (ISR; 177), rash (137), pyrexia (116), vomiting (57), urticaria (55), pain (43), headache (43) and nausea (32).

Of the total 177 cases of ISR, 53% (94) were in those aged ≥7 years. More than half the cases of rash (79; 58%) and pyrexia (69; 59%) were reported in those aged <7 years.

There were 20 reports of anaphylaxis: five in children aged <5 years, 10 in individuals aged 20 to <65 years, and two in individuals aged ≥65 years (three had missing age). Eleven (55%) of these had received seasonal influenza vaccine.

There were 17 reported cases of syncope and 11 cases of presyncope during 2019. Ninety-four per cent (16) of cases of syncope and 64% (7) of cases of presyncope were reported in persons aged ≥7 years.

There were seven reports of hypotonic-hyporesponsive episode (HHE) and all were reported in children <2 years of age. The children had all received DTPa-IPV-HepB-Hib, 13vPCV and rotavirus vaccines, with the exception of one child who received DTPa-IPV-HepB-Hib and meningococcal B vaccines.

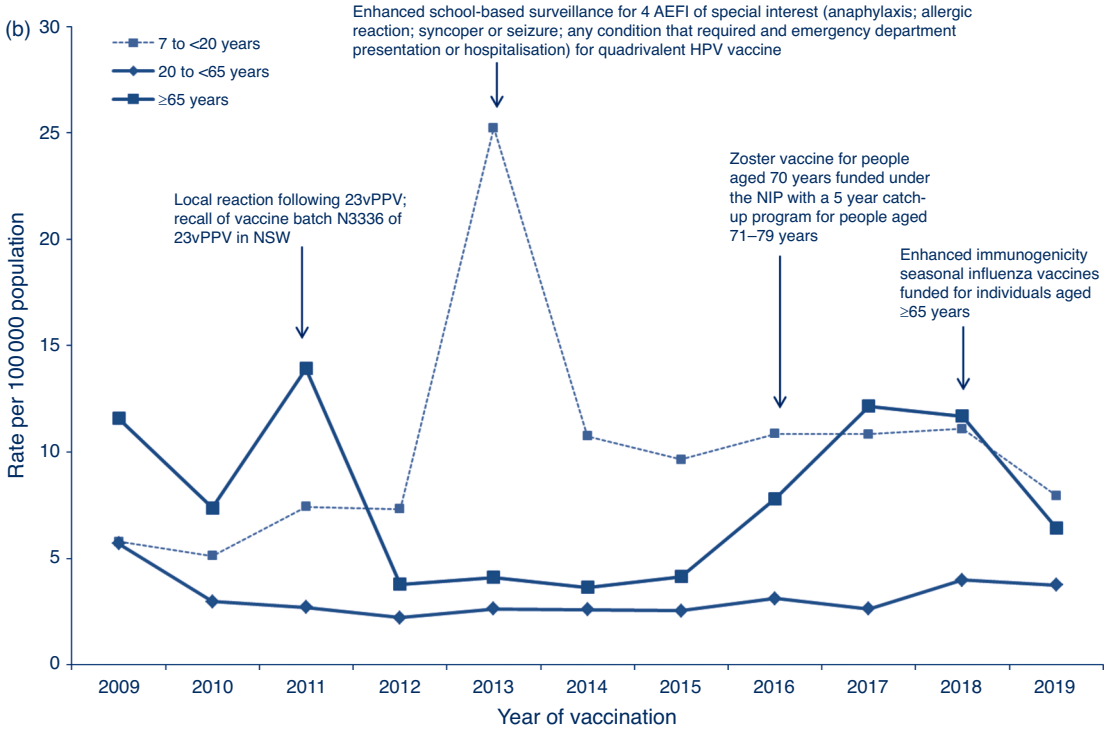

Figure 4b. Reporting rates of adverse events following immunisation for NSW per 100 000 population, 2009–2019, for people aged ≥7 years, by year of vaccination.

NB: 23vPPV batch N3336 was recalled in March 2011; the TGA implemented enhanced school-based surveillance for four acute AEFI of special interest in 2013 in collaboration with state and territory health departments; zoster vaccine was NIP funded for people aged 70 years with a catch up program for people aged 71–79 years; and enhanced immunogenicity trivalent seasonal influenza vaccines were NIP funded for people aged ≥65 years in April 2018.

Source: Adverse Events Management System database, Therapeutic Goods Administration.

There were four cases of Guillain-Barre syndrome (GBS), all in people who had received seasonal influenza vaccines; two of these cases developed symptoms within 21 days of influenza vaccination. Two GBS cases also reported upper respiratory tract infection or influenza-like illness prior to hospital presentation.

There were two cases of intussusception reported in children aged <1 year within 14 days of rotavirus vaccination.

Approximately 14% of reported events (90) were recorded as serious in 2019, a decrease compared with 2018, when 200 events (24%) were recorded as serious. Adverse events recorded as 'serious' included pyrexia (17), rash (13), anaphylaxis (13), ISR (9), convulsions (9) and others, as shown in Table 3. Sixty-three per cent of convulsions (5) recorded as serious were febrile convulsions in children aged <7 years.

Death in 2019

One death was reported to NSW Health following complications from suspected GBS. A 75-year-old male with comorbidities (syndrome of inappropriate antidiuretic hormone secretion and fluctuating blood pressure) died in late September 2019, several months after receiving adjuvanted trivalent seasonal influenza vaccine and 23vPPV a week apart in May 2019. The patient presented to a GP in July 2019 with unsteady and slow gait and hip and lower back pain, and was transferred to hospital for respiratory support for hypoxic respiratory failure, with deteriorating respiratory function due to difficulty clearing secretions and weak cough. The principal diagnoses and causes of his death were aspiration pneumonitis, GBS and emphysema. The death met the temporal criteria for a serious AEFI, and the timing of the vaccination and clinical findings are consistent with a possible relationship to vaccination.

Discussion

Adverse event reporting rates have generally increased over the past decade. This is partly due to having more population-wide vaccination programs (increasing the number of vaccines administered per person) and partly due to efforts to improve reporting to NSW Health and the TGA. AEFI reporting is encouraged in order to monitor the safety of all vaccines used. Notably, from 2018 to 2019 there was a statistically significant decrease in the overall estimated population-based AEFI rate, as well as a decrease in the proportion of serious AEFI.

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, 2019

Vaccine[a]	AEFI records[b] 2019	Serious[c] 2019	Reporting rate per 100 000 doses[d] 2019	
	n	*n*	Rate	(95% CI)
<7 years				
13vPCV	81	13	29.4	(23.4–36.6)
DTPa-IPV-HepB-Hib	78	13	28.4	(22.5–35.5)
DTPa-IPV	67	4	68.6	(53.2–87.2)
Rotavirus	56	10	31.8	(24.0–41.3)
MMR	47	8	46.2	(34.0–61.5)
Seasonal influenza	39	8	15.1	(10.7–20.6)
DTPa	38	6	40.1	(28.4–55.1)
Meningococcal ACWY	37	7	34.6	(24.4–47.7)
Hib	26	6	29.5	(19.3–43.2)
MMRV	24	4	25.3	(16.2–37.6)
Meningococcal B	14	1	22.3	(12.2–37.5)
Hepatitis B	4	1	45.0	(12.3–115.2)
Hib-MenC	2	1	75.6	(9.2–273.0)
Varicella	2	1	66.1	(8.0–238.8)
12–17 years				
HPV	46	4	26.4	(19.3–35.2)
dTpa	33	5	36.0	(24.8–50.5)
Seasonal influenza	7	0	9.0	(3.6–18.5)
Meningococcal ACWY	5	1	6.7	(2.2–15.6)
MMR	2	0	43.8	(5.3–158.1)
Varicella	2	0	84.5	(10.2–305.2)
18–64 years				
Seasonal influenza	126	16	15.0	(12.5–17.9)
dTpa	24	2	13.7	(8.8–20.4)
Meningococcal B	14	5	395.3	(216.1–663.2)
23vPPV	10	0	69.4	(33.3–127.6)
Hepatitis B	10	4	16.2	(7.8–29.8)
MMR	9	2	16.9	(7.7–32.1)
Meningococcal ACWY	6	1	49.5	(18.2–107.7)
Yellow fever	1	1	9.0	(0.2–50.2)
≥65 years				
Seasonal influenza	44	5	5.8	(4.2–7.7)
Zoster	25	1	47.8	(30.9–70.5)
23vPPV	24	3	24.3	(15.6–36.2)
dTpa	7	0	19.7	(7.9–40.6)

AEFI, adverse events following immunisation.
[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 2019 and 31 December 2019. More than one vaccine may be coded as 'suspected' if several were administered at the same time.
[c]'Serious' is defined in the Methods section.
[d]The estimated AEFI reporting rate per 100 000 vaccine doses recorded.
Source: Adverse Events Management System database, Therapeutic Goods Administration.

Several vaccines were associated with the decrease in the overall estimated population-based AEFI rate in 2019 compared with 2018. The number of AEFI records for seasonal influenza vaccine decreased by 18% overall (from 282 to 232), and by 53% (from 93 to 44) in adults aged ≥65 years, despite the total number of influenza vaccine doses distributed increasing in recent years, from approximately 1.3–1.5 million doses per year from 2014 to

Table 2. Vaccine types listed as 'suspected' in records of adverse events following immunisation (AEFI), NSW, 2019

Suspected vaccine type	AEFI records		One suspected vaccine only[a]		'Serious'		Age group[b] <7 years		Age group[b] ≥7 years	
	n	(%)	*n*	(%)[c]	*n*	(%)[c]	*n*	(%)[c]	*n*	(%)[c]
Seasonal influenza	232	(34.8)	198	(85)	33	(14)	39	(17)	188	(81)
13vPCV	82	(12.3)	0	(0)	13	(16)	81	(99)	1	(1)
DTPa-IPV-HepB-Hib	78	(11.7)	21	(27)	13	(17)	78	(100)	0	(0)
DTPa-IPV	70	(10.5)	66	(94)	5	(7)	67	(96)	2	(3)
dTpa	67	(10.1)	27	(40)	7	(10)	0	(0)	67	(100)
MMR	59	(8.9)	16	(27)	10	(17)	47	(80)	11	(19)
Rotavirus	56	(8.4)	8	(14)	10	(18)	56	(100)	0	(0)
HPV	52	(7.8)	21	(40)	4	(8)	0	(0)	52	(100)
Meningococcal ACWY	50	(7.5)	8	(16)	9	(18)	37	(74)	13	(26)
DTPa	38	(5.7)	10	(26)	6	(16)	38	(100)	0	(0)
23vPPV	36	(5.4)	19	(53)	4	(11)	1	(3)	35	(97)
Meningococcal B	29	(4.4)	17	(59)	6	(21)	14	(48)	15	(52)
Hib	28	(4.2)	0	(0)	7	(25)	26	(93)	1	(4)
Zoster	28	(4.2)	20	(71)	1	(4)	0	(0)	28	(100)
MMRV	27	(4.1)	5	(19)	5	(19)	24	(89)	2	(7)
Hepatitis B	14	(2.1)	7	(50)	5	(36)	4	(29)	10	(71)
Varicella	9	(1.4)	5	(56)	1	(11)	2	(22)	7	(78)
Hepatitis A-typhoid	5	(0.8)	4	(80)	1	(20)	0	(0)	5	(100)
Hepatitis A	4	(0.6)	2	(50)	0	(0)	1	(25)	3	(75)
Typhoid	4	(0.6)	0	(0)	0	(0)	0	(0)	4	(100)
Rabies	3	(0.5)	3	(100)	0	(0)	0	(0)	3	(100)
dT	2	(0.3)	2	(100)	0	(0)	0	(0)	2	(100)
Hib-MenC	2	(0.3)	0	(0)	1	(50)	2	(100)	0	(0)
Yellow fever	2	(0.3)	1	(50)	1	(50)	0	(0)	2	(100)
BCG	1	(0.2)	1	(100)	1	(100)	0	(0)	0	(0)
dTpa-IPV	1	(0.2)	0	(0)	0	(0)	0	(0)	1	(100)
Hepatitis A and B	1	(0.2)	1	(100)	0	(0)	0	(0)	1	(100)
IPV	1	(0.2)	1	(100)	0	(0)	0	(0)	1	(100)
Japanese encephalitis	1	(0.2)	1	(100)	0	(0)	0	(0)	1	(100)
MenCCV	1	(0.2)	0	(0)	0	(0)	0	(0)	1	(100)
Total[d]	666	(100.0)	466	(70)	90	(14)	289	(43)	366	(55)

[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. seasonal influenza was 'suspected' in 232 AEFI records; this was the only suspected vaccine in 85% of the 232 AEFI records, 14% were defined as 'serious' and 81% 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 Events Management System database, Therapeutic Goods Administration.

2017, to 2.3 million doses in 2018 and 2.5 million doses in 2019 (Health Protection NSW, personal communication). This was a statistically significant decrease in the reporting rate per 100 000 doses for 2019 (5.8, 95% CI 4.2–7.7 per 100 000 doses) compared with 2018 (14.6, 95% CI 11.8–17.9 per 100 000 doses) in adults aged ≥65 years. Two enhanced immunogenicity trivalent influenza vaccines, Fluad® and Fluzone® High-Dose, were introduced to the NIP for people aged ≥65 years in 2018,[25] and the number of AEFI records for seasonal influenza vaccines in this group increased from 28 in 2017 to 93 in 2018. In 2019, both vaccines were available, but only Fluad® was NIP-funded. In 2018 active surveillance data indicated that this vaccine brand was associated with a slightly lower AEFI rate compared with Fluzone® High-Dose,[14,26] which, along with increased provider and consumer familiarity, may in part explain the decrease in AEFI records for seasonal influenza vaccines in this group in 2019.

Table 3. Selected reported adverse events[a] as classified predominantly by MedDRA Preferred Terms in records of adverse events following immunisation (AEFI), NSW, 2019[b]

MedDRA Preferred Terms (adverse events)	AEFI records	Only adverse event reported[c]		'Serious'		Age group[d] <7 years		Age group[d] ≥7 years	
	n	*n*	(%)[e]	*n*	(%)[e]	*n*	(%)[e]	*n*	(%)[e]
Injection site reaction[f]	177	87	(49)	9	(5)	83	(47)	94	(53)
Rash[g]	137	54	(39)	13	(9)	79	(58)	57	(42)
Pyrexia	116	6	(5)	17	(15)	69	(59)	47	(41)
Vomiting	57	4	(7)	7	(12)	35	(61)	21	(37)
Urticaria	55	17	(31)	7	(13)	27	(49)	27	(49)
Headache	43	0	(0)	6	(14)	5	(12)	37	(86)
Pain	43	1	(2)	4	(9)	9	(21)	34	(79)
Nausea	32	0	(0)	3	(9)	1	(3)	31	(97)
Pruritus	30	1	(3)	3	(10)	4	(13)	26	(87)
Dizziness	27	0	(0)	2	(7)	0	(0)	26	(96)
Malaise	27	0	(0)	2	(7)	6	(22)	21	(78)
Diarrhoea	25	2	(8)	4	(16)	13	(52)	11	(44)
Extensive limb swelling	23	10	(43)	3	(13)	16	(70)	7	(30)
Chills	21	0	(0)	1	(5)	2	(10)	19	(90)
Paraesthesia	21	0	(0)	5	(24)	1	(5)	20	(95)
Anaphylaxis	20	13	(65)	13	(65)	5	(25)	12	(60)
Myalgia	20	0	(0)	0	(0)	1	(5)	19	(95)
Convulsions[h]	19	13	(68)	9	(47)	14	(74)	5	(26)
Lethargy	18	0	(0)	1	(6)	9	(50)	9	(50)
Decreased appetite	17	0	(0)	3	(18)	13	(76)	4	(24)
Dyspnoea	17	0	(0)	4	(24)	3	(18)	13	(76)
Swelling	17	0	(0)	3	(18)	6	(35)	11	(65)
Syncope	17	7	(41)	2	(12)	1	(6)	16	(94)
Pallor	16	1	(6)	3	(19)	10	(63)	6	(38)
Cough	15	0	(0)	3	(20)	5	(33)	8	(53)
Irritability	15	0	(0)	2	(13)	15	(100)	0	(0)
Chest discomfort	14	0	(0)	0	(0)	0	(0)	14	(100)
Fatigue	14	0	(0)	2	(14)	1	(7)	13	(93)
Erythema	13	1	(8)	1	(8)	5	(38)	8	(62)
Presyncope	11	6	(55)	1	(9)	4	(36)	7	(64)
Angioedema	10	1	(10)	0	(0)	4	(40)	6	(60)
Rhinorrhoea	10	0	(0)	0	(0)	4	(40)	6	(60)
Abdominal pain	9	0	(0)	0	(0)	3	(33)	6	(67)
Oropharyngeal discomfort	9	0	(0)	3	(33)	1	(11)	8	(89)
Somnolence	9	0	(0)	0	(0)	5	(56)	4	(44)
Flushing	8	0	(0)	0	(0)	4	(50)	4	(50)
Lymphadenopathy	8	1	(13)	0	(0)	2	(25)	6	(75)
Apnoea	7	0	(0)	0	(0)	7	(100)	0	(0)
Bradycardia	7	0	(0)	1	(14)	7	(100)	0	(0)
Chest pain	7	0	(0)	1	(14)	0	(0)	7	(100)
Hyperhidrosis	7	0	(0)	1	(14)	3	(43)	4	(57)
Hypotonic hyporesponsive episode	7	4	(57)	2	(29)	7	(100)	0	(0)
Tachycardia	7	0	(0)	1	(14)	0	(0)	7	(100)
Injected limb mobility decreased	6	0	(0)	0	(0)	1	(17)	5	(83)
Haematochezia	5	2	(40)	0	(0)	5	(100)	0	(0)

Hypoaesthesia	5	0	(0)	1	(20)	0	(0)	5	(100)
Arthralgia	4	1	(25)	1	(25)	0	(0)	4	(100)
Guillain-Barre syndrome	4	3	(75)	4	(100)	1	(25)	3	(75)
Asthenia	3	0	(0)	2	(67)	0	(0)	2	(67)
Lymphadenitis	3	1	(33)	0	(0)	1	(33)	2	(67)
Intussusception	2	1	(50)	2	(100)	2	(100)	0	(0)

[a]A complete list of adverse events as classified by individual Preferred Terms is available on request.
[b]Selected reported adverse events reported during January 2019–December 2019. Note: for injection site reaction, rash and convulsions, preferred terms were grouped as described below.
[c]AEFI records where only one adverse event was reported.
[d]Not shown if neither age nor date of birth were recorded.
[e]Percentages relate to the number of AEFI records in which the specific adverse event term was listed.
[f]Injection site reaction MedDRA codes included injection site reaction, injection site swelling, injection site pain, injection site mass, injection site erythema, injection site cellulitis, injection site induration, injection site abscess sterile, injection site discharge, injection site necrosis, injection site nodule, injection site urticaria, vaccination site movement impairment, vaccination site streaking, administration site erythema and administration site induration.
[g]Rash MedDRA codes included rash, rash erythematous, rash generalised, rash maculo-papular, rash macular, rash vesicular, rash papular, rash morbilliform and rash pruritic.
[h]Convulsion MedDRA codes included febrile convulsion, seizure, status epilepticus and tonic convulsion.
Source: Adverse Events Management System database, Therapeutic Goods Administration.

Among people aged 7–19 years, there were fewer AEFI records for meningococcal ACWY vaccine in 2019 (10 records) compared with 2018 (39 records). This was a statistically significant decrease in the reporting rate per 100 000 doses for 2019 (6.7, 95% CI 2.2–15.6 per 100 000 doses) compared with 2018 (29.2, 95% CI 20.3–40.6 per 100 000 doses). The observed decline may reflect the time since the introduction of funded MenACWY vaccine; although the MenACWY vaccine was introduced to the NIP for adolescents and young adults aged 15–19 years in 2019, a state-funded program was established in NSW in 2017 (in that year, AEFI records increased to 34 from 0 in 2016).

There was also a 26% decrease in the number of AEFI records for DTPa-IPV from 2018 to 2019, especially in children aged 2 to <7 years (91 records in 2018 to 67 records in 2019). However, the rate per 100 000 DTPa-IPV doses was not significantly different for children aged <7 years in 2019 (68.6, 95% CI 53.2–87.2 per 100 000 doses) compared with 2018 (96.8, 95% CI 78.2–118.5 per 100 000 doses).

ISR, rash and pyrexia were the most commonly reported adverse events in 2019. There was a decrease in the number of AEFI reports overall from 2018 to 2019, and for individual adverse events including ISR (from 259 to 177), influenza like illness (from 20 to 4) and angioedema (from 26 to 10). However, there was an increase in the number of reports for some adverse events, including anaphylaxis, which increased from 12 reports in 2018 to 20 reports in 2019. This is likely due to a change in the way reports of anaphylaxis were coded by the TGA from 2018 onwards, using Brighton Collaboration Case Definition Criteria.[27] AusVaxSafety, an active sentinel vaccine safety surveillance system, also monitored the safety of select vaccines in 2019 and found no safety signals, including for influenza vaccines in all ages.[28]

A limitation of our report was interpretation of the serious code for all reported adverse events, which is primarily used as a guide for sponsor reporting. As it is not necessarily based on verified clinical data, it may not capture all medically important events and is unlikely to be robust. Another limitation is that the information collated in the AEMS database is intended primarily to detect safety signals in relation to 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, stimulated reporting and the variable quality and completeness of information provided in individual notifications.[12] Finally, the AEFI reported here are not necessarily causally related to vaccination; they may be coincidental or may be caused by a vaccine(s), or during handling or administration.

Conclusion

Overall, the total number of reported AEFI decreased during 2019 compared with 2018. The majority of AEFI 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.

Acknowledgements

We thank Alexandra Hendry, NCIRS, for providing vaccine dose data from the Australian Immunisation Register.

The National Centre for Immunisation Research and Surveillance is supported by the Australian Government Department of Health, Health Protection NSW and The Children's Hospital at Westmead.

References

1. Council for International Organizations of Medical Sciences (CIOMS) c/o World Health Organization. Definition and Application of Terms for Vaccine Pharmacovigilance: Report of CIOMS/WHO Working Group on Vaccine Pharmacovigilance. 2012.
2. Lawrence G, Boyd I, McIntyre P, Isaacs D. Surveillance of adverse events following immunisation: Australia 2002 to 2003. *Commun Dis Intell* 2004; 28(3): 324–338. Y 20/9/10.
3. Lawrence G, Boyd I, McIntyre P, Isaacs D. Annual report: surveillance of adverse events following immunisation in Australia. *Commun Dis Intell* 2005; 30(3): 319–333. Y 27/9/10.
4. Lawrence G, Gold MS, Hill R, Deeks S, Glasswell A, McIntyre PB. Annual report: surveillance of adverse events following immunisation in Australia. *Commun Dis Intell* 2007; 32(4): 371–387.
5. Lawrence GL, Aratchige PE, Boyd I, McIntyre PB, Gold MS. Annual report on surveillance of adverse events following immunisation in Australia. *Commun Dis Intell* 2006; 31(3): 269–282.
6. Lawrence GL, Boyd I, McIntyre PB, Isaacs D. Annual report: surveillance of adverse events following immunisation in Australia. *Commun Dis Intell* 2004; 29(3): 248–262. Y 23/9/10.
7. Menzies R, Mahajan D, Gold MS, Roomiani I, McIntyre P, Lawrence G. Annual report: surveillance of adverse events following immunisation in Australia. *Commun Dis Intell* 2008; 33(4): 365–381.
8. Mahajan D, Campbell-Lloyd S, Cook J, Menzies R. NSW annual report describing adverse events following immunisation, 2010. *NSW Public Health Bull* 2011; 22(9–10): 196–208.
9. Mahajan D, Campbell-Lloyd S, Roomiani I, Menzies R. NSW Annual Adverse Events following immunisation report, 2009. *NSW Public Health Bull* 2010; 21(9–10): 224–233.
10. Mahajan D, Cook J, Dey A, Macartney K, Menzies RI. Annual report: surveillance of adverse events following immunisation in Australia, 2011. *Commun Dis Intell* 2012; 36(4): E315–32. Y 13/2/12.
11. Mahajan D, Cook J, McIntyre PB, Macartney K, Menzies RI. Annual report: surveillance of adverse events following immunisation in Australia, 2010. *Commun Dis Intell* 2011; 35(4): 263–280. Y 14/5/12.
12. Mahajan D, Reid S, Cook J, Macartney K, Menzies R. NSW annual report describing adverse events following immunisation, 2011. *NSW Public Health Bull* 2012; 23(9–10): 187–200.
13. National Health and Medical Research Council. The Australian Immunisation Handbook. 8th edn. Australian Government Department of Health and Ageing; 2003.
14. Australian Technical Advisory Group on Immunisation (ATAGI). Australian Immunisation Handbook, Australian Government Department of Health, Canberra. Accessed 17 January 2019, https://beta.health.gov.au/resources/publications/the-australian-immunisation-handbook
15. Uppsala Monitoring Centre. WHO Collaborating Centre for International Drug Monitoring. Accessed 9 July 2014, http://www.who-umc.org/
16. Brown EG, Wood L, Wood S. The medical dictionary for regulatory activities (MedDRA). *Drug Saf* 1999; 20(2): 109–117.
17. Zhou W, Pool V, Iskander JK, English-Bullard R, Ball R, Wise RP *et al*. Surveillance for safety after immunization: Vaccine Adverse Event Reporting System (VAERS) – United States, 1991–2001. [erratum appears in MMWR Morb Mortal Wkly Rep. 2003 Feb 14; 52(06): 113]. *MMWR Surveill Summ* 01 24/2003; 52(1): 1–24.
18. SAS Institute Inc. The SAS system for Windows [computer program]. Version 9.4. Cary, N.C. 2012.
19. StataCorp. Stata Statistical Software: Release 14. https://www.stata.com/
20. R Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing. https://www.R-project.org/
21. Australian Bureau of Statistics. Estimated Resident Population by Single Year of Age, New South Wales [Data cube]. Accessed 28 September, 2020. https://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3101.0Jun% 202019
22. Hull B, Hendry A, Dey A, Macartney K, McIntyre P, Beard F. Exploratory analysis of the first 2 years of adult vaccination data recorded on AIR. National Centre for Immunisation Research and Surveillance; 2019.
23. Dey A, Wang H, Quinn H, Nicholl S, Hill R, Macartney K. Surveillance of adverse events following immunisation, NSW, 2014. NSW Health. Accessed 21 October 2016, http://www.health.nsw.gov.au/immunisation/Documents/2014-NSW-AEFI-report.pdf
24. Dey A, Wang H, Quinn H, Reid S, Cook J, Macartney K. Surveillance of adverse events following immunisation, NSW, 2015. NSW Health. Accessed 17 September 2018, https://www.health.nsw.gov.au/immunisation/Documents/2015-NSW-AEFI-report.pdf
25. Australian Technical Advisory Group on Immunisation (ATAGI). Statement on the administration of seasonal influenza vaccines in 2018. Australian Government Department of Health. https://www.health.gov.au/resources/publications/atagi-advice-on-seasonal-influenza-vaccines-in-2018
26. Australian Technical Advisory Group on Immunisation (ATAGI). Statement on the administration of seasonal influenza vaccines in 2019. Australian Government Department of Health. https://www.health.gov.au/resources/publications/atagi-advice-on-seasonal-influenza-vaccines-in-2019
27. Rüggeberg JU, Gold MS, Bayas J *et al*. Anaphylaxis: case definition and guidelines for data collection, analysis, and presentation of immunization safety data. *Vaccine* 2007; 25(31): 5675–5684.
28. National Centre for Immunisation Research and Surveillance. AusVaxSafety. Accessed 1 November 2019, http://www.ausvaxsafety.org.au/