Annual reports

Annual report: surveillance of adverse events following immunisation in Australia, 2008

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Abstract

This report summarises Australian passive surveillance data for adverse events following immunisation (AEFI) reported to the Therapeutic Goods Administration (TGA) for 2008, and describes reporting trends over the 9-year period 2000 to 2008. There were 1,542 AEFI records for vaccines administered in 2008. This was an annual AEFI reporting rate of 7.2 per 100,000 population, a 5% decrease compared with 2007. The majority of AEFI reports described non-serious events while 10% (n = 152) were classified as serious. Two deaths temporally associated with immunisation were reported; there was no evidence to suggest a causal association. The most commonly reported reactions were injection site reaction, allergic reaction, fever and headache. AEFI reporting rates in 2008 were 2.7 events per 100,000 administered doses of influenza vaccine for adults aged ≥18 years, 18.9 per 100,000 administered doses of pneumococcal polysaccharide vaccine for those aged ≥65 years, and 17.2 per 100,000 administered doses of scheduled vaccines for children aged <7 years. Reports for infants increased in 2008, mainly related to gastrointestinal system events temporally associated with receipt of rotavirus vaccine in the 1st full year of the rotavirus immunisation program, while there was a substantial decrease in AEFI reports for human papillomavirus vaccine in adolescents compared with 2007 when the program commenced. Increases in reports in children and adults were also partly attributed to the implementation of enhanced passive surveillance in Victoria. The consistently low reporting rate of serious AEFI highlights the safety of vaccines in Australia and illustrates the value of the national TGA database as a surveillance tool for monitoring AEFIs nationally. *Commun Dis Intell* 2009;33(4):365–381.

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

Introduction

The aim of passive post-licensure surveillance of adverse events following immunisation (AEFI) is to monitor the vaccine and immunisation program safety. An 'adverse event following immunisation' is defined as any serious or unexpected adverse event that occurs *after* a vaccine has been given, which may be related to the vaccine itself or to its handling or administration. An AEFI can be *coincidentally* associated with the *timing* of immunisation without necessarily being caused by the vaccine or the immunisation process. Analysing trends in passive reports can identify signals or assist in generating hypotheses that can then be tested by more rigorous methods. This can lead to the detection of population-specific, rare, late-onset or unexpected adverse events that have not been identified in pre-licensure vaccine trials.[1,2]

Several important changes to vaccine funding and availability occurred in 2007 and 2008 that impact on the AEFI surveillance data presented in this report. These are:

- In March 2008, Queensland, South Australia and Victoria changed from using 2 combination vaccines (i.e. quadrivalent DTPa-IPV and Hib-HepB) to the single hexavalent DTPa-IPV-HepB-Hib vaccine for children at 2, 4 and 6 months of age,[3-6] due to an international shortage of some *Haemophilus influenzae* type b (Hib) vaccines (PedvaxHib® [monovalent] and Comvax® [Hib-HepB]).[7] The hexavalent vaccine has been used in all other jurisdictions since November 2005, except for all infants in the Northern Territory and Indigenous infants in Western Australia, who continue to receive pentavalent DTPa-IPV-HepB and monovalent Hib vaccines.
- The national rotavirus immunisation program commenced in July 2007, when rotavirus (RotaTeq® and Rotarix®) vaccines were added to the National Immunisation Program (NIP) for all infants in Australia.[8] This followed the earlier introduction in the Northern Territory in October 2006. Infants receive either a 2-dose schedule (Rotarix®) at 2 and 4 months of age, or a 3-dose schedule (RotaTeq®) at 2, 4 and 6 months of age.
- The national human papillomavirus (HPV) immunisation program commenced in April 2007 for all girls aged 12–18 years, and was extended to the 19–26 year age group in July 2007.[8] Two vaccines are funded—the quadrivalent vaccine (Gardasil®) and the bivalent vaccine (Cervarix®). Both vaccines are given as a 3-dose course.

Previous changes to the NIP schedule[8-10] also impact on the interpretation of trend data, and have been described in detail in previous reports published regularly since 2003.[11-21] These are: (i) in 2003, the commencement of the meningococcal C conjugate vaccine (MenCCV) immunisation program and the removal of the 18-month dose of DTPa vaccine; (ii) from 2004, the progressive introduction of a dose of dTpa for adolescents;[9] (iii) in January 2005, the commencement of the 7-valent pneumococcal conjugate vaccine (7vPCV) program for infants and the 23-valent polysaccharide vaccine (23vPPV) for adults aged ≥65 years;[7,8] and (iv) in November 2005, varicella for infants and at 12–13 years of age for those with no evidence of previous vaccination or varicella infection, and the replacement of oral poliovirus vaccine with inactivated poliovirus vaccine (IPV) for children. All IPV-containing vaccines include diphtheria-tetanus-acellular pertussis (DTPa) antigens (i.e. quadrivalent vaccines) and some also include hepatitis B (HepB) and/or *Haemophilus influenzae* type b (Hib) antigens (i.e. pentavalent and hexavalent vaccines). The specific combination vaccines administered at 2, 4, and 6 months of age vary between states and territories but all jurisdictions provide DTPa-IPV quadrivalent vaccine at 4 years of age.[10]

Methods

AEFI are notified to the Therapeutic Goods Administration (TGA) by state and territory health departments, health professionals, vaccine manufacturers and members of the public.[9,10] All reports are assessed using internationally consistent criteria[22] and entered into the Australian Adverse Drug Reactions System (ADRS) database. All reports for vaccines and complementary medicines, plus all serious reports for drugs, are forwarded to the Adverse Drug Reactions Advisory Committee (ADRAC) for review at regular meetings. This is an expert committee of the TGA composed of independent medical experts who have expertise in areas of importance to the evaluation of medicine safety.

Adverse events following immunisation data

De-identified information on AEFI reports from the ADRS database for vaccine adverse event notifications received to 28 February 2009, were released to the National Centre for Immunisation Research and Surveillance (NCIRS). Readers are referred to previous AEFI surveillance reports for a description of the surveillance system and methods used to evaluate reports to the TGA.[12,13] This report focuses on AEFI reported for vaccines administered during 2008 and trends in AEFI reporting for the 9-year period 2000 to 2008.

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 and *either*

a. the vaccination occurred between 1 January 2000 and 31 December 2008 *or*
b. for records where the vaccination date was not recorded, the date of onset of symptoms or signs occurred between 1 January 2000 and 31 December 2008.

Study definitions of adverse events following immunisation outcomes and reactions

AEFI were defined as 'serious' or 'non-serious' based on information recorded in the ADRS database and criteria similar to those used by the World Health Organization[22] and the US Vaccine Adverse Events Reporting System (VAERS).[23] In this report, an AEFI is defined as 'serious' if the record indicated that the person had recovered with sequelae, been admitted to a hospital, experienced a life-threatening event, or died.

The causality ratings of 'certain', 'probable' and 'possible' are assigned to individual AEFI records by the TGA and reviewed by ADRAC. They describe the likelihood that a suspected vaccine or vaccines was/were associated with the reported reaction at the level of the individual vaccine recipient. Factors that are considered in assigning causality ratings include the timing (minutes, hours etc) and the spatial correlation (for injection site reactions) of symptoms and signs in relation to vaccination, and whether one or more vaccines were administered, and are outlined in more detail elsewhere.[12] Because children in particular receive several vaccines at the same time, all administered vaccines are usually listed as 'suspected' of involvement in a systemic adverse event as it is usually not possible to attribute the AEFI to a single vaccine.

Typically, each AEFI record listed several symptoms, signs and diagnoses that had been re-coded by TGA staff from the reporter's description into standardised terms using the Medical Dictionary for Regulatory Activities (MedDRA®).[24] AEFI reports of suspected anaphylaxis and hypotonic-hyporesponsive episodes (HHE) were reviewed

* The term 'AEFI record' is used throughout this report because a single AEFI notification to the Medicine Safety Monitoring Unit can 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.

† Records are classified as 'suspected' if the report contains sufficient information to be valid and the relationship between reported reactions and drugs are not deemed as biologically implausible.

by ADRAC and classified using the Brighton Collaboration case definitions.[25,26] If an AEFI report met any level of the Brighton Collaboration case definition it was coded accordingly.

To analyse reported AEFI, we grouped MedDRA® coding terms to create a set of reaction categories. Firstly, reaction categories were created that were analogous to the AEFI listed and defined in *The Australian Immunisation Handbook* (9th edition). Additional categories were created for MedDRA® coding terms that were listed in more than 1% of AEFI records (e.g. headache, dizziness, change in heart or respiratory rate or rhythm). Reaction terms listed in less than 1% of records were grouped into broader categories based on the organ system where the reaction was manifested (e.g. gastrointestinal, neurological).

Data analysis

All data analyses were performed using SAS software version 9.1.3.[27] The distribution of AEFI records was analysed by age, sex and jurisdiction. Average annual population-based reporting rates were calculated for each state and territory and by age group using population estimates obtained from the Australian Bureau of Statistics.

The frequency and age distribution of reported AEFI outcomes, reaction categories and vaccines were assessed. For each vaccine, the age distribution of vaccinees was calculated, as well as the proportion of records where (i) the vaccine was the only suspected vaccine or drug; (ii) the AEFI record was assigned a 'certain' or 'probable' causality rating; and (iii) the AEFI was defined as 'serious'.

AEFI reporting rates per 100,000 administered doses were estimated for influenza vaccine for adults aged ≥18 years; for 23vPPV for adults aged ≥65 years; and for 10 vaccines funded through the NIP for children aged < 7 years. The 2008 AEFI reporting rates were compared with those for 2007 and 2006.

Denominator data to estimate influenza and 23vPPV AEFI reporting rates were obtained from the national adult coverage survey conducted in 2006 (unpublished) for adults aged ≥65 years and 18–64 years (influenza only). The number of administered doses of each of the 10 childhood vaccines was calculated from the Australian Childhood Immunisation Register (ACIR), a national population-based register of approximately 99% of children aged < 7 years.[28]

Dose-based AEFI reporting rates could not be calculated for other vaccines and age groups as reliable denominator data for the number of vaccine doses distributed or administered were not available.

Notes on interpretation

Caution is required when interpreting the AEFI 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 2008. Data published in previous reports for 2000–2007[11-21] differ to that presented in this report for the same period because the data have been updated to include AEFI notified to the TGA after original publication.

The information collated in the ADRS database is intended primarily for signal detection and hypothesis generation. While AEFI reporting rates can be estimated using appropriate denominators, such as the number of vaccine doses administered, they cannot be interpreted as incidence rates due to under-reporting and biased reporting of suspected AEFI, and the variable quality and completeness of information provided in individual AEFI notifications.[11–21,29]

It is important to note that this report is based on vaccine and reaction term information collated in the ADRS database and not on comprehensive clinical notes. Individual database records list symptoms, signs and diagnoses that were used to define a set of reaction categories based on the case definitions provided in the 9th edition of *The Australian Immunisation Handbook*.[10] These reaction categories are similar, but not identical, to the AEFI case definitions.

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. The causality ratings assigned to individual AEFI records describe the likelihood that a suspected vaccine or vaccines was/were associated with the reported reaction in an individual vaccine recipient.

Results

Summary of data

There was a total of 1,542 AEFI records in the ADRS database where the date of vaccination (or onset of an adverse event, if vaccination date was not reported) occurred between 1 January and 31 December 2008. This was 5% lower than in 2007. In 2008, approximately 2% of AEFI notifications resulted in more than 1 AEFI record in the database, usually an injection site reaction (ISR) and a systemic reaction.

Of the 1,542 AEFI records, 152 (10%) were defined as 'serious' (i.e. recovery with sequelae, requiring hospitalisation, experiencing a life-threatening event or death). A total of 440 (29%) AEFI records were assigned causality ratings of 'certain' (n = 380, 25%) or 'probable' (n = 60, 4%).

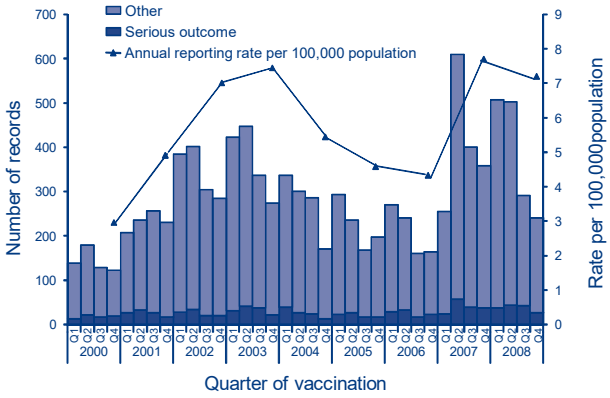
Reporting trends

The AEFI reporting rate for 2008 was 7.2 per 100,000 population, compared with 7.7 per 100,000 population in 2007 (Figure 1). This is the third highest reporting rate for the period 2000 to 2008, and is similar to the peaks in 2003 and 2007 that coincided with the national MenCCV and HPV programs, respectively. The trends in AEFI notifications shown in Figure 1 are reflected in the trends in vaccines frequently suspected of involvement in reported AEFI (Figure 2), and in the types of reactions frequently reported (Figure 3).

Many of these changes correspond in time with changes in the funded NIP schedule. Most recently, the previously mentioned addition of HPV and rotavirus vaccines in 2007 and the change over for Queensland, South Australia and Victoria to the hexavalent DTPa-IPV-HepB-Hib vaccine for infants in March 2008. Previously, reporting rates increased then stabilised at lower rates following the introductions of 7vPCV in 2005 and MenCCV in 2003 (Figure 2). Following this trend, reports for HPV vaccine peaked in the year of that vaccine's introduction in 2007 and declined substantially in 2008 (Figure 2).

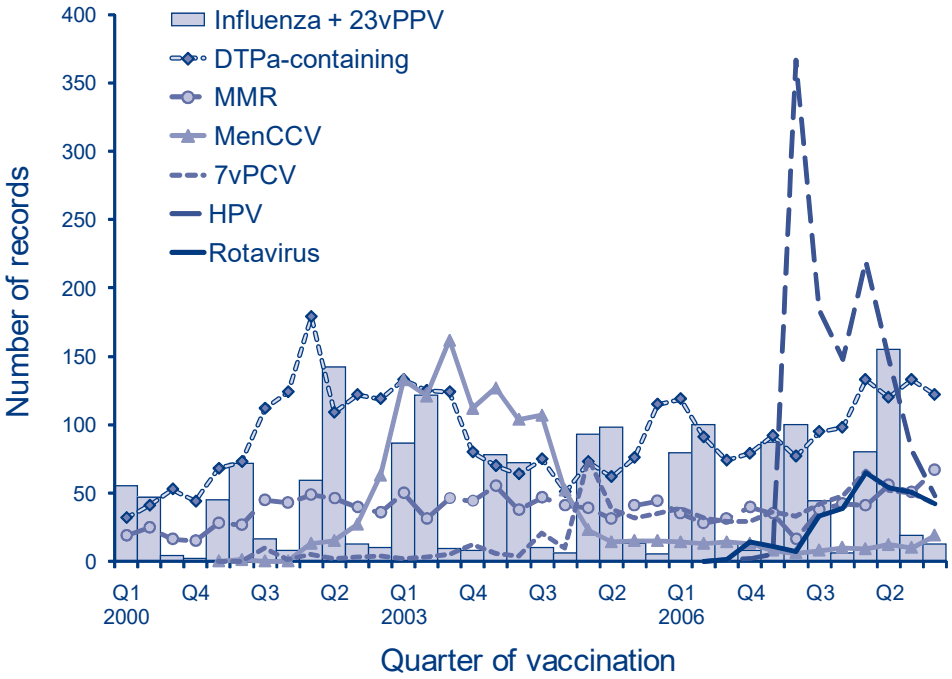
The usual seasonal pattern of AEFI reporting, with peaks in the first half of the year, was also apparent in 2008 (Figure 1). The seasonal peaks generally correspond to the months when more vaccinations are administered in Australia, particularly among 4– and 5-year-old children receiving MMR and DTPa-containing vaccines prior to commencing school in February and older Australians receiving 23vPPV and influenza vaccine during the autumn months (March to June) (Figure 2).

Figure 1: Adverse events following immunisation, ADRS database, 2000 to 2008, by quarter of vaccination



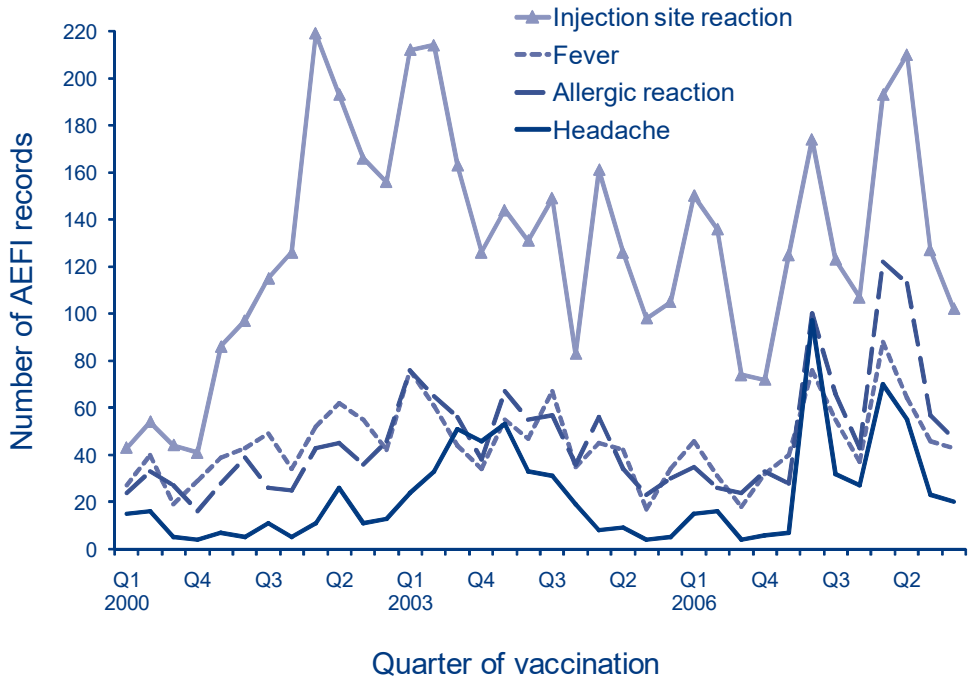
For reports where the date of vaccination was not recorded, the date of onset was used as a proxy for vaccination date.

Figure 2: Frequently suspected vaccines, adverse events following immunisation, ADRS database, 2000 to 2008, by quarter of vaccination



See appendix for abbreviations of vaccine names. DTPa-containing vaccines include DTPa, and the combination vaccines DTPa-HepB, DTPa-IPV, DTPa-IPV-HepB and DTPa-IPV-HepB-Hib.

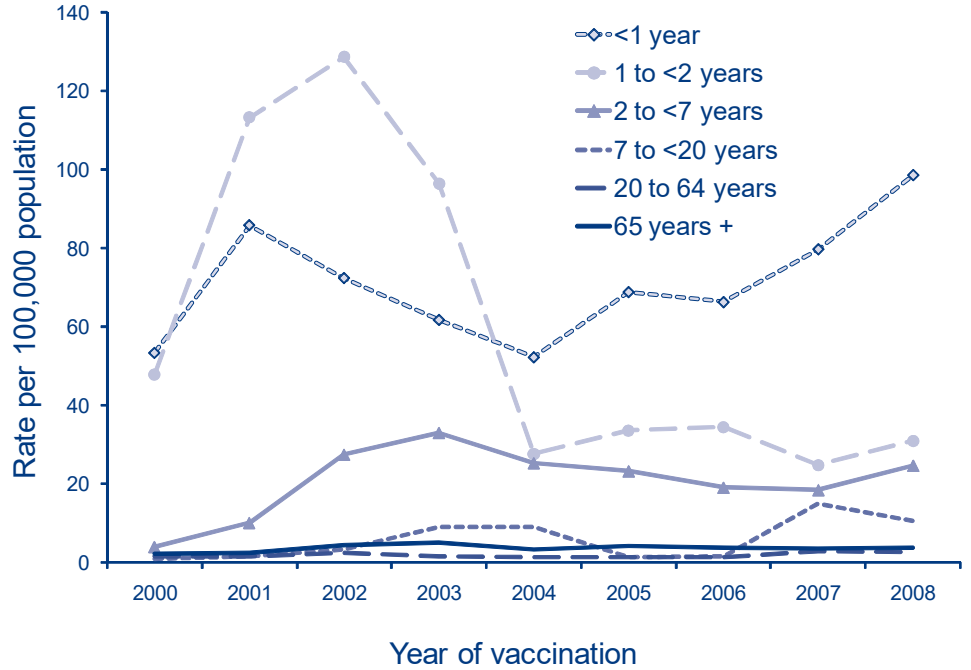
Figure 3: Selected frequently reported adverse events following immunisation, ADRS database, 2000 to 2008, by quarter of vaccination



Age distribution

In 2008, the highest population-based AEFI reporting rate occurred in infants < 1 year of age, the age group that received the highest number of vaccines (Figure 4). Compared with 2007, AEFI reporting rates increased among the < 1 year age group (24% increase from 79.6 to 98.5 per 100,000 population), the 1 to < 2 year age group (25%, 24.7 to 30.8 per 100,000) and the 2 to < 7 year age group (34%, 18.4 to 24.6 per 100,000). Rates declined for older children and adolescents (30%, 14.8 to 10.4 per 100,000) and remained stable for adults (2.89 to 2.82 per 100,000).

Figure 4: Reporting rates of adverse events following immunisation per 100,000 population, ADRS database, 2000 to 2008, by age group and year of vaccination



Geographical distribution

As reported previously,[12,13,16,18-20] AEFI reporting patterns varied between states and territories for vaccines received during 2008 (Table 1). The Northern Territory, the Australian Capital Territory and South Australia had the highest reporting rates (19.1, 17.1 and 15.3 per 100,000 population, respectively) while Western Australia and New South Wales had the lowest rates (4.7 per 100,000 population). AEFI reporting rates decreased in all jurisdictions in 2008 except Victoria and Tasmania. The increase in Victoria (from 3.7 per 100,000 in 2006 to 6.7 in 2007 and 8.9 in 2008) followed the implementation of a new AEFI reporting and evaluation system in that state in April 2007.[30]

Outcomes

Sixty per cent of reported AEFI in 2008 were defined as 'non-serious' while 10% were defined as 'serious' (Table 2), similar to the proportions observed in previous years. Fewer 'serious' AEFI were assigned certain or probable causality ratings compared with 'non-serious' AEFI (12% versus 29%) (Table 2). Numbers of reported AEFI and AEFI with outcomes defined as 'serious' are shown in Table 3.

Two deaths were recorded as temporally associated with receipt of vaccines. One was a 22-month-old child who had received varicella vaccine 18 days prior to death. The cause of death was reported to be intracranial haemorrhage secondary to idiopathic thrombocytopenia (ITP), which was diagnosed 10 days after receipt of the vaccine. While temporally related to vaccine administration, no causal relationship has been established. The second reported death was a 1-year-old child who had received Hib, meningococcal C and MMR vaccines. The cause of death was reported to be cerebral oedema due to encephalitis 12 days after receipt of the vaccine, with onset of illness 10 days after vaccination. According to the treating neurologist and paediatrician it was unlikely to be vaccine related.

Vaccines

The 1,542 AEFI records for 2008 listed 31 different vaccines as suspected of involvement in the reported AEFI (Table 3). The percentage of records where only 1 vaccine was reported differed by vaccine, as did the percentage assigned causality ratings of 'certain' or 'probable', and with outcomes defined as 'serious'. This is to be expected because vaccines are routinely co-administered at specific ages in the immunisation schedule.

The most frequently reported individual vaccine was HPV with 497 records (32%) (Table 3). Vaccines containing diphtheria, tetanus and acellular pertussis antigens (including combination vaccines and dTpa) were suspected in 547 (35%) records (Table 3),

Table 1: Adverse events following immunisation (AEFI), ADRS database, 1 January to 31 December 2008, by state or territory

State or territory	AEFI records		Annual reporting rate per 100,000 population*			
	n	%	Overall	'Certain' or 'probable' causality rating†	'Serious' outcome‡	Aged <7 years
Australian Capital Territory	59	4	17.1	3.8	0.6	95.0
New South Wales	325	21	4.7	1.4	0.5	10.6
Northern Territory	42	3	19.1	10.0	1.8	51.5
Queensland	222	14	5.2	1.9	0.6	19.8
South Australia	246	16	15.3	3.9	0.9	93.8
Tasmania	31	2	6.2	2.6	0.4	34.0
Victoria	472	31	8.9	2.3	0.7	65.7
Western Australia	103	7	4.7	1.1	0.7	28.4
Other§	42	3	na	na	na	na
Total	1,542	100	7.2	2.1	0.7	36.7

* Average annual rates per 100,000 population calculated using mid-2008 population estimates (Australian Bureau of Statistics).

† See previous report[12] for criteria used to assign causality ratings.

‡ AEFI records defined as 'serious' (i.e. recovery with sequelae, hospitalisation, life-threatening or death – see Table 2).

§ Records where the jurisdiction in which the AEFI occurred was not reported or was unclear. AEFI records in this category were notified by pharmaceutical companies (n=27), members of the public (11), and general practitioners (4).

Table 2: Outcomes of adverse events following immunisation (AEFI), ADRS database, 2008

Outcome	AEFI records		'Certain' or 'probable' causality rating*		Age group†			
					<7 years		≥7 years	
	n	%‡	n	%§	n	%§	n	%§
Non-serious	919	60	264	29	400	44	513	56
Not recovered at time of report	285	18	88	31	110	39	172	60
Not known (missing data)	186	12	70	38	93	50	89	48
Serious	152	10	18	12	96	63	55	36
recovered with sequelae	2		0		1		1	
hospital treatment – admission	146		18		93		53	
life-threatening event	2		0		0		1	
death (maybe drug)	2		0		3		0	
Total	1,542	100	440	29	699	45	829	54

* Causality ratings were assigned to AEFI records using criteria described previously.[12]

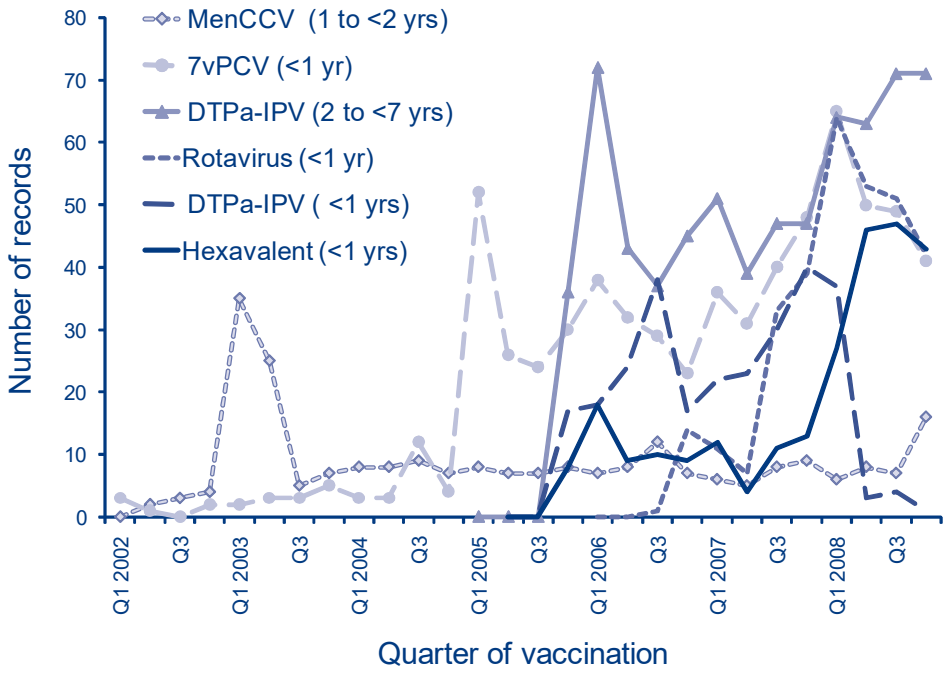
† AEFI records where both age and date of birth were not recorded are not shown (14 missing).

‡ Percentages relate to the total number of AEFI records (n = 1,542).

§ Percentages relate to the number of AEFI records with the specific outcome, e.g. of 919 AEFI records with a 'non-serious' outcome, 29% had causality ratings of 'certain' or 'probable' and 44% were for children aged <7 years.

with DTPa-IPV (320 records; 21%) and hexavalent DTPa-IPV-HepB-Hib (169 records; 11%) the most frequently reported vaccines in this group. In the <1 year age group, reports that included DTPa-IPV decreased and reports of DTPa-IPV-HepB-Hib increased, in line with the changes in usage of those vaccines as outlined in the Introduction (Figure 5). The other frequently reported vaccines were MMR

Figure 5: Reports of adverse events following immunisation, ADRS database, 2002 to 2008, for vaccines recently introduced into the funded National Immunisation Program,* by quarter of vaccination



* Meningococcal C conjugate vaccine (MenCCV) was introduced into the NIP on 1 January 2003, 7-valent pneumococcal conjugate vaccine (7vPCV) on 1 January 2005, both DTPa-IPV and hexavalent vaccines on 1 November 2005, and rotavirus vaccine on 1 July 2007.

Table 3: Vaccine types listed as 'suspected' in records of adverse events following immunisation (AEFI), ADRS database, 2008

Suspected vaccine type*	AEFI records	One suspected vaccine or drug only†		'Certain' or 'probable' causality rating‡		'Serious' outcome§		Age group‖			
								< 7 years		≥ 7 years	
	n	n	%¶	n	%¶	n	%¶	n	%¶	n	%¶
HPV**	497	440	89	110	22	35	7	1	0.2	493	99
DTPa-IPV	320	149	47	137	43	18	6	314	98	2	1
MMR	215	32	14	22	10	15	7	205	95	8	4
Rotavirus††	212	48	23	17	8	50	24	211	99	0	–
7vPCV	210	6	3	5	2	39	19	209	99	0	–
DTPa-IPV-HepB-Hib	169	12	7	9	5	29	17	169	100	0	–
Influenza	160	119	74	30	19	12	8	22	14	135	84
23vPPV	137	94	69	64	47	11	8	14	10	121	88
Hepatitis B	74	25	34	7	9	7	9	3	4	71	96
Hib-Hepatitis B	63	3	5	1	2	10	16	63	100	0	–
Varicella	57	37	65	11	19	11	19	37	65	20	35
MenCCV	50	2	4	3	6	6	12	49	98	1	2
dTpa	44	26	59	14	32	1	2	0	–	43	98
Hib	33	0	–	2	6	5	15	32	97	1	3
dT	15	11	73	6	40	0	–	0	–	15	100
Hepatitis A	15	2	13	1	7	3	20	10	67	5	33
DTPa	11	6	55	2	18	4	36	11	100	0	–
Hepatitis A + B	8	5	63	3	38	2	25	0	–	8	100
Hepatitis A-Typhoid	6	1	17	0	–	0	–	1	17	5	83
IPV	6	1	17	0	–	0	–	3	50	3	50
Yellow fever	6	3	50	0	–	0	–	0	–	6	100
BCG	4	4	100	4	100	0	–	3	75	1	25
DTPa-IPV-HepB	3	0	–	0	–	1	33	3	100	0	–
Typhoid	3	0	–	0	–	2	67	1	33	2	67
Cholera	2	2	100	0	–	1	50	0	–	2	100
Rabies	2	2	100	0	–	0	–	0	–	2	100
Q fever	2	1	50	1	50	0	–	0	–	2	100
Japanese encephalitis	1	1	100	0	–	0	–	0	–	1	100
Tetanus	1	1	100	0	–	1	100	0	–	1	100
dTpa-IPV	0	0	–	0	–	0	–	0	–	0	–
Men4PV	0	0	–	0	–	0	–	0	–	0	–
Total‡‡	1,542	419	27	440	29	152	10	699	45	829	54

* See appendix for abbreviations of vaccine names.

† AEFI records where only one vaccine was suspected of involvement in a reported adverse event.

‡ Causality ratings were assigned to AEFI records using criteria described previously.[12]

§ 'Serious' outcomes are defined in the Methods section (see also Table 2).

‖ AEFI records are not shown if both age and date of birth were not reported.

¶ 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 497 AEFI records; this was the only suspected vaccine in 89% of the 497 AEFI records, 22% had 'certain' or 'probable' causality ratings, 7% were defined as 'serious' and 99% were for those aged ≥7 years.

** Human papillomavirus vaccine was added to the National Immunisation Program schedule on 1 April 2007.[8]

†† Rotavirus vaccine was added to the National Immunisation Program schedule on 1 July 2007.[8]

‡‡ 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.

(215 records; 14%), rotavirus (212 records; 14%) and 7vPCV (210 records; 14%).

AEFI reporting trends differed by vaccine. In 2008, compared with 2007, reports were substantially reduced for HPV (497 in 2008 vs 705 in 2007) and Hib-HepB (63 vs 118) vaccines, while reports increased for DTPa-IPV (320 vs 28), MMR (215 vs 131), 23vPPV (137 vs 118), DTPa-IPV-HepB-Hib (169 vs 139), 7vPCV (210 vs 159) and rotavirus (212 vs 90) (Figure 2). As previously reported there were peaks in AEFI reporting for individual vaccines soon after their introduction into the routine childhood immunisation schedule, followed by a reduction and stabilisation in reporting over time (Figure 2). This pattern was particularly evident for MenCCV in 2003, 7vPCV and DTPa-IPV containing vaccines in 2005, and HPV vaccine in 2007 (Figures 2 and 5), while a decrease in reports for rotavirus vaccine, which commenced later in 2007, was not evident.

Reports for rotavirus vaccines increased in total number as well as rate (41.0 per 100,000 doses in 2008 compared with 33.2 per 100,000 in 2007; Table 4). The majority of the cases (45.3%) were reported from Victoria. Thirty-six per cent of the total 212 rotavirus vaccine AEFI reports list rotavirus as the only vaccine suspected of involvement in the reported adverse event while the majority (64%) listed other vaccines as well, which is to be expected as most infants now receive rotavirus vaccine at the same time as other scheduled vaccines at 2, 4 and 6 months of age.

Reactions

The distribution and frequency of reactions listed in AEFI records for 2008 are shown in Tables 5 and 6. In Table 5, only the reaction categories analogous to those listed in *The Australian Immunisation Handbook*[10] are shown. In Table 5, other reaction categories are listed in descending order of frequency.

Table 4: Reporting rates of adverse events following immunisation (AEFI) per 100,000 vaccine doses,* children aged less than 7 years, ADRS database, 2008

	AEFI records‡ (n)	Vaccine doses* (n)	Reporting rate per 100,000 doses§ 2008	2007	2006
Vaccine†					
DTPa-containing vaccines	486	1,079,244	45.0	33.1	32.3
DTPa-IPV	314	342,757	91.6	45.3	43.0
Pentavalent (DTPa-IPV-HepB)	3	17,347	17.3	44.1	37.4
Hexavalent (DTPa-IPV-HepB-Hib)	169	719,140	23.5	10.7	12.9
Haemophilus influenzae type b	32	165,897	19.3	17.7	22.1
Haemophilus influenzae type b-hepatitis B	63	162,439	38.8	30.7	24.8
Measles-mumps-rubella	205	540,872	37.9	23.2	24.4
Meningococcal C conjugate	49	292,738	16.7	11.6	18.4
Pneumococcal conjugate	209	825,447	25.3	20.6	15.8
Rotavirus vaccine	211	514,659	41.0	45.0	-
Varicella	37	264,891	14.0	10.6	18.5
Age group					
<1 year	279	2,250,276	12.4	9.7	8.6
1 to <2 years	79	1,022,447	7.7	6.2	9.3
2 to <7 years	304	573,464	53.0	38.6	39.5
AEFI category†					
Total	662	3,846,187	17.2	13.3	13.9
'Certain' or 'probable' causality rating	191	3,846,187	5.0	4.2	5.4
'Serious' outcome	89	3,846,187	2.3	1.6	1.4

* Number of vaccine doses recorded on the Australian Childhood Immunisation Register (ACIR) and administered between 1 January and 31 December 2008.

† Records where at least one of the vaccines shown in the table was suspected of involvement in the reported adverse event. AEFI category includes all records (i.e. total), those assigned 'certain' or 'probable' causality ratings, and those with outcomes defined as 'serious'. Causality ratings were assigned using the criteria described previously.[12] A 'serious' outcome is defined as recovery with sequelae, hospitalisation, life-threatening event or death.[12]

‡ 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 and 31 December 2008. More than one vaccine may be coded as 'suspected' if several were administered at the same time.

§ The estimated AEFI reporting rate per 100,000 vaccine doses recorded on the ACIR.

Table 5: Reaction categories of interest* mentioned in records of adverse events following immunisation (AEFI), ADRS database, 2008

Reaction category*	AEFI records	Only reaction reported†		'Certain'/'probable' causality rating‡		Age group§			
						<7 years		≥ 7 years	
	n	n	%‖	n	%‖	n	%‖	n	%‖
Injection site reaction	632	170	27	322	51	325	51	301	48
Allergic reaction¶	360	51	14	53	15	119	33	238	66
Fever	241	5	2	11	5	124	51	117	49
Rash**	131	39	30	18	14	72	55	56	43
Syncope	74	10	14	22	30	8	11	66	89
Abnormal crying	57	2	4	6	11	57	100	-	
Convulsions	43	7	16	10	23	24	56	19	44
Arthralgia	41	2	5	4	10	-		40	98
HHE††	39	14	36	1	3	39	100	-	
Lymphadenopathy/itis‡‡	33	7	21	5	15	5	15	28	85
Intussusception	14	10	71	0		14	100	-	
Abscess	10	5	50	7	70	9	90	1	10
Anaphylactic reaction	5	-		1	20	2	40	3	60
Guillain-Barré syndrome	4	4	100	1	25	1	25	2	50
Parotitis	4	1	25	-		1	25	3	75
Thrombocytopenia	4	1	25	1	25	2	50	2	50
Arthritis	3	1	33	-		-		3	100
Brachial neuritis	2	-		-		-		2	100
Death	2	-		-		2	100	-	
Encephalitis	2	-		-		1	50	1	50
Encephalopathy	1	-		-		1	100	-	
Acute flaccid paralysis	-	-		-		-		-	
Meningitis	-	-		-		-		-	
Orchitis	-	-		-		-		-	
Osteitis	-	-		-		-		-	
Osteomyelitis	-	-		-		-		-	
Sepsis	-	-		-		-		-	
SSPE§§	-	-		-		-		-	
Toxic shock syndrome	-	-		-		-		-	
Total‖‖	1,542	419	27	440	29	699	45	829	54

* Reaction categories were created for the AEFI of interest listed and defined in *The Australian Immunisation Handbook,* (9th edition, p 58–65 and 360–3)[10] as described in Methods section.

† AEFI records where only one reaction was reported.

‡ Causality ratings were assigned to AEFI records using criteria described previously.[12]

§ Not shown if neither age nor date of birth were recorded.

‖ Percentages relate to the number of AEFI records in which the specific reaction term was listed, e.g. of 632 AEFI records listing injection site reaction, 27% listed only one type of reaction while 51% had a causality rating of 'certain' or 'probable' and 51% were for children aged <7 years.

¶ Allergic reaction includes skin reactions including pruritus, urticaria, periorbital oedema, facial oedema, erythema multiforme etc. and/or gastrointestinal (e.g. diarrhoea, vomiting) symptoms and signs but does not include other abdominal symptoms like abdominal pain, nausea, flatulence, abnormal faeces, hematochezia etc.[10]

** includes general terms of rash but does not include rash pruritic.

†† Hypotonic-hyporesponsive episode.

‡‡ Includes lymphadenitis following BCG vaccination and the more general term of 'lymphadenopathy'.

§§ Subacute sclerosing panencephalitis.

‖‖ 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 reaction term.

Table 6: 'Other'* reaction terms listed in records of adverse events following immunisation (AEFI), ADRS database, 2008

Reaction category*	AEFI records	Only reaction reported†		'Certain'/'probable' causality rating‡		Age group§			
						<7 years		≥ 7 years	
	n	n	%‖	n	%‖	n	%‖	n	%‖
Headache	168	4	2	23	14	5	3	162	96
Malaise	161	1	1	19	12	30	19	130	81
Nausea	130	-		16	12	6	5	124	95
Dizziness	88	-		17	19	1	1	87	99
Gastrointestinal – RVV¶	66	11	17	10	15	66	100	-	
Respiratory rate/rhythm change	64	9	14	1	2	33	52	31	48
Irritability	63	-		4	6	61	97	2	3
Reduced sensation	62	2	3	10	16	-		62	100
Myalgia	59	1	2	2	3	-		59	100
Pain	56	1	2	10	18	1	2	55	98
Pallor	48	-		8	17	22	46	26	54
Abdominal pain	39	-		4	10	10	26	29	74
Somnolence	36	1	3	5	14	20	56	16	44
Erythema	31	2	6	2	6	19	61	10	32
Heart rate/rhythm change	30	-	-	4	13	14	47	16	53
Anorexia	25	1	4	1	4	15	60	10	40
Weakness	25	1	4	4	16	2	8	23	92
Oedema	23	-	-	6	26	4	17	19	83
Flushing	21	1	5	5	24	5	24	16	76
Increased sweating	19	-		4	21	4	21	15	79
Tremor	17	-		2	12	2	12	15	88
Other	382	41	11	52	14	125	33	255	67
eye or ear	55	4	7	10	18	10	18	43	78
neurological	54	12	22	5	9	13	24	41	76
respiratory	47	3	6	6	13	14	30	33	70
Gastrointestinal**	41	7	17	6	15	21	51	20	49
psychological	34	3	9	5	15	9	26	25	74
cardiovascular	30	2	7	7	23	8	27	22	73
general non-specific	29	1	3	7	24	8	28	21	72
Skin††	28	4	14	5	18	10	36	18	64
musculoskeletal	26	1	4	1	4	4	15	22	85
infection	22	2	9	2	9	6	27	16	73
metabolic/endocrine	17	-		-		8	47	9	53
renal/urogenital	16	3	19	3	19	2	12	14	88
haematological	10	1	10	-		2	20	8	80
miscellaneous	3	-		1	33	1	33	2	67
pregnancy/congenital	3	1	33	1	33	1	33	2	67

* Reaction terms not listed in *The Australian Immunisation Handbook*[10] but included in AEFI records in the ADRAC database. The top part of the table shows reaction terms included in 1% or more of AEFI records; the bottom part of the table shows reaction terms, grouped by organ system, that were included in less than 1% of AEFI records.

† AEFI records where only one reaction was reported.

‡ Causality ratings were assigned to AEFI records using criteria described previously.[12]

§ Not shown if neither age nor date of birth were recorded.

‖ Percentages relate to the number of AEFI records in which the specific reaction term was listed, e.g. of 632 AEFI records listing injection site reaction, 27% listed only one type of reaction while 51% had a causality rating of 'certain' or 'probable' and 51% were for children aged <7 years.

¶ Gastrointestinal – RVV includes all the GI reactions following rotavirus vaccination.

** Other, gastrointestinal does not include GI reactions and gastrointestinal – RVV signs and symptoms.

†† Other, skin includes purpura, petechie, blister, burning, dermatitis, dry skin etc, but does not include skin reactions.

The most frequently reported adverse events were injection site reaction (ISR; 41% of 1,542 AEFI records) followed by allergic reaction (23%), fever (16%), headache (11%), malaise (10%) rash (9%) and nausea (9%) (Tables 5 and 6). ISR was the most commonly reported individual adverse event following receipt of DTPa-IPV (81%; 259/320), 23vPPV (89%; 122/137), MMR (63%; 135/215), all DTPa-containing vaccines (55%; 301/547), and influenza vaccine (39%; 63/160), administered alone or in combination with other vaccines. Twenty-three per cent (113/497) of HPV vaccine-related AEFI records listed ISR.

More severe AEFI included reports of convulsion (n = 43), HHE (n = 39), anaphylactic reaction (n = 5), Guillain-Barré syndrome (GBS; n = 4), thrombocytopenia (n = 4), death (n = 2; described previously in this report) and encephalitis (n = 2).

There was a total of 43 reports of convulsion, including syncopal and febrile convulsions. Twenty-three were for children aged < 7 years and 40% of reports were from Victoria. The most commonly suspected vaccines were HPV (n = 13), 7vPCV (n = 8), rotavirus (n = 6) and MMR (n = 6). The majority (30/39) of HHE were notified by Victoria (22) and South Australia (8). DTPa-containing vaccines were listed as suspected in 38 reports, with hexavalent DTPa-IPV-HepB-Hib suspected in 23 reports and DTPa-IPV in 13 reports. 7vPCV (n = 33), rotavirus (n = 32) and Hib-HepB (n = 10) were also commonly suspected vaccines in HHE reports. Two of the 5 reports of anaphylaxis in 2008 occurred in adolescent girls following receipt of HPV vaccine,[31] while the other reports occurred following receipt of DTPa-IPV/MMR in a child, HepB in an adult, and DTPa-IPV-HepB-Hib /7vPCV in an infant. The 4 records coded as GBS included 3 reports in adults aged ≥60 years following influenza vaccine and 1 report following DTPa-IPV and MMR vaccine in a child.

Reactions shown in Table 6 include headache, malaise, nausea and dizziness. Many of the reaction terms shown in this table were reported for HPV and rotavirus vaccines.

Reactions mentioned in less than 1% of AEFI records in 2008 are shown in the lower portion of Table 6, grouped by organ system categories. The most commonly reported categories were coded as 'gastrointestinal and 'neurological'.

The trends in the most frequently reported types of reactions have changed over time (Figure 3). Reports of headache and allergic reactions peaked in 2003 and again in 2007, coinciding with the national school-based MenCCV immunisation program in 2003 and the HPV program in 2007. Much of the variation in reporting of ISR relates to specific changes in the immunisation schedules for vaccines that are known to have higher rates of ISR, including DTPa-containing vaccines, MenCCV, 23vPCV and HPV vaccine.[11-21,32,33] Increases in reports of fever in 2007 and 2008 are associated with both new vaccines added to the NIP in that period – rotavirus and HPV.

Dose-based adverse events following immunisation reporting rates

Influenza vaccine and adults aged ≥ 18 years

In 2008, influenza vaccine was suspected in 127 AEFI records for people aged ≥18 years. Using the 2006 estimate of the number of doses of vaccine administered to people aged ≥ 65 years, the AEFI reporting rate was 2.7 per 100,000 administered doses, slightly higher than the rate in 2006 and 2007 (Table 7). As seen in previous years, the overall AEFI reporting rates were higher for vaccinees aged 18–64 years than among older vaccinees. However, there was a drop in the serious AEFI reporting rate in the 18–64 year age group during 2008 (Table 7). The most frequently reported adverse events were ISR, allergic reaction, fever, malaise and nausea (1.2, 0.7, 0.5, 0.3 and 0.3 per 100,000 doses, respectively). Reporting rates for each of these reactions were higher in the 18–64 year age group. There were 4 reports of GBS following influenza vaccination in 2008 giving a reporting rate of 0.1 per 100,000 doses. This is higher than in recent years, when only 1 or 2 reports were received annually,[16,18] but well within the expected reporting rates.

Pneumococcal vaccine and adults aged ≥ 65 years

There were 81 AEFI reports for older adults that included 23vPPV, with 5 reports coded as serious and 75 reports of ISR. Using the 2006 estimate of the number of doses of 23vPPV administered to people aged ≥ 65 years (n = 429,500), the AEFI reporting rate was 18.9 per 100,000 doses, with 1.2 serious and 17.5 ISR reports per 100,000 doses. This is similar to the rate reported for 2007 (18.6 per 100,000 doses with 1.4 serious).[20]

Scheduled vaccines for children aged < 7 years

There was a total of 699 AEFI records for children aged < 7 years for vaccines administered in 2008. This was a 33% increase on the 526 AEFI records during 2007, which was the highest since 2003 when there were 485 AEFI records.

Of the total AEFI records in 2008, 662 records included one of the 10 vaccines for which ACIR data could be used to estimate AEFI reporting rates per 100,000 administered doses (Table 4). Vaccines for which reliable denominator data were not available included bacille Calmette-Guérin (n = 3), influenza (n = 22), 23vPPV (n = 14), hepatitis A (n = 10) and

Table 7: Reporting rate of adverse events following immunisation (AEFI) per 100,000 doses of influenza vaccine,* 18 years and over, ADRS database, 2008

AEFI category†	Age group	AEFI records‡ (n)	Vaccine doses* (n)	Rate per 100,000 doses§		
				2008	2007	2006
Overall	≥18 years	127	4,746,900	2.7	2.3	1.9
	18 to 64 years	90	2,626,400	3.4	3.0	2.5
	≥65 years	37	2,120,500	1.7	1.4	1.1
Serious	≥18 years	9	4-,746,900	0.2	0.3	0.2
	18 to 64 years	5	2,626,400	0.2	0.4	0.3
	≥65 years	4	2,120,500	0.2	0.1	0.1

* Number of administered doses of influenza vaccine estimated from the 2006 national survey (unpublished).

† AEFI category includes all records, and those defined as 'serious' where influenza vaccine was suspected of involvement in the reported adverse event. The definition of a 'serious' outcome is given in the Methods section.

‡ Number of AEFI records in which influenza vaccine was 'suspected' and the vaccination was administered in 2008.

§ The estimated reporting rate of adverse events per 100,000 administered doses of influenza vaccine.

hepatitis B (n = 3) (Table 3). The overall reporting rate for the 10 NIP vaccines was 17.2 per 100,000 administered doses, while the reporting rate for serious AEFI was 2.3 per 100,000 doses (Table 4). AEFI reporting rates were higher than for the same period in 2007 for most age groups, reaction categories and vaccines (Table 4), while the rates of AEFI with certain or probable causality ratings remained stable.

The largest changes were for DTPa-IPV, hexavalent (DTPa-IPV-HepB-Hib), Hib-HepB and measles-mumps-rubella (MMR) vaccines. There was a substantial increase (42%) in the reporting in children aged < 7 years in Victoria, which predominantly included reports of non-serious events (60.2%). The main suspected vaccines included DTPa-IPV (n = 168), DTPa-IPV-HepB-Hib (n = 75), MMR (n = 102), 7vPCV (n = 20) and rotavirus (n = 96).

Reporting rates for the different DTPa-IPV combination vaccines varied by vaccine type and age group. The reporting rate for pentavalent DTPa-IPV-HepB vaccine is likely to be inaccurate due to the small number of reports and some under-reporting to the ACIR of doses administered.

The very high reporting rate for DTPa-IPV vaccine (91.6 per 100,000 doses) include both children aged < 1 year who were scheduled to receive the vaccine at 2, 4, and 6 months of age (53.1 per 100,000 doses) and the 2 to < 7 year age group (106 per 100,000 doses) (Table 4). The majority of the AEFI reports for the older age group following DTPa-IPV listed ISR (97 per 100,000 doses compared with 63 per 100,000 doses in 2007), and the increase from Victoria accounted for 83% of the national increase. This is the highest reporting rate for ISR following DTPa-containing vaccines since 2002.

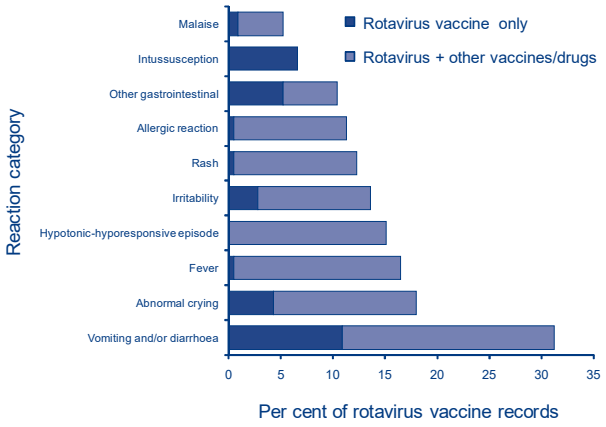
The overall AEFI reporting rate for children aged < 1 year was higher for quadrivalent DTPa-IPV compared with the hexavalent DTPa-IPV-HepB-Hib vaccine (53.1 vs 23.1 reports per 100,000 administered doses) (Table 4). The majority (73%) of the AEFI reports for quadrivalent DTPa-IPV for children aged < 1 year came from Victoria (reporting rate 79.6 per 100,000 doses), but within Victoria the reporting rate for DTPa_IPV was greater than for hexavalent DTPa-IPV-HepB-Hib vaccine (reporting rate 48.3 per 100,000 doses). Reporting rates among infants for most reaction categories were approximately 2 to 3 times higher for DTPa-IPV, except for HHE, which was 5-fold higher for DTPa-IPV (15.3 per 100,000 doses) compared with DTPa-IPV-HepB-Hib (3.3 per 100,000 doses).

The most commonly reported AEFIs following rotavirus vaccine were diarrhoea and vomiting (31%; n = 66) followed by abnormal crying (17.9%; n = 38), fever (17%; n = 35) and HHE (15%; n = 32). There were 14 (6.6%) reports of intussusception in 2008 (2.7 per 100,000 administered doses) compared with eight in 2007 (3.6 per 100,000 doses) (Figure 6).

Discussion

The AEFI reporting rate in 2008 was the third highest in the period covered by this analysis (since 2000) and slightly lower than in 2007. The majority of AEFI reported to the TGA in 2008 were mild, transient and well-recognised vaccine side effects. The percentage of serious AEFI remained stable at 9%–10%. The main features of AEFI reporting in 2008, compared with previous years, were an overall increase in reports from Victoria, an increase in

Figure 6: Most frequently reported adverse events following rotavirus immunisation,* ADRS database, 2008, by number of vaccines suspected of involvement in the reported adverse event



* Percentage of 212 AEFI records where rotavirus vaccine was listed as suspected of involvement in the reported AEFI

children by 30%–40% and in adults by 10%–20%, and a reduction in AEFI reporting for HPV among adolescents.

The increases appear to be at least partly due to reporting from the first full year of enhanced passive surveillance in Victoria, as well as reports associated with rotavirus vaccine in the first full calendar year since its inclusion in the NIP. Nearly one in 3 AEFI reports (31%) during 2008 were received from a single jurisdiction, Victoria (n = 472), and the reporting rate in that jurisdiction increased 30% since 2007 and 140% since 2006. The jurisdiction with the next highest number of reports in 2008 was New South Wales (n = 325), followed by South Australia (n = 246) and Queensland (n = 222). This increase in reporting rate demonstrates the effectiveness of the methods used to enhance passive surveillance in Victoria, which could also be applied in jurisdictions with less sensitive reporting systems. At present, comparisons between jurisdictions to detect program errors or effects of different vaccines are complicated by the differences in the reporting methods. Developing and maintaining high rates of AEFI reporting from all states and territories is important for the integrity of a national database.

In children < 1 year of age the most commonly reported vaccines were rotavirus, hexavalent DTPa-IPV-HepB-Hib vaccine, 7vPCV and Hib-HepB and the reaction categories included diarrhoea and vomiting, abnormal crying, HHE and rash. The increase is likely to relate to the implementation of the rotavirus immunisation program in July 2007 as well as improvements in the sensitivity of surveillance in Victoria. Rotavirus vaccine is co-administered with 7-valent pneumococcal conjugate vaccine and combination vaccines containing DTPa, IPV, Hib and HepB antigens, and therefore increases in reports for one of these vaccines will be reflected in reports for the others as well.

The most commonly reported AEFI following rotavirus vaccine were gastrointestinal symptoms, predominantly diarrhoea and vomiting (31%) followed by fever (17%) and HHE (15%) and there were 14 reports of intussusception. The majority (10/14) of intussusception reports were infants after dose 1 (2–3 months age group) and 4 cases after dose 2 (4–5 months age group). No deaths occurred among reported intussusception cases. Of the 14 intussusception reports, 10 cases (71%) occurred in infants within 1–30 days after vaccination, including 7 cases (50%) that occurred within 1–7 days after vaccination. This is substantially lower than the 53 cases detected in a study by the Australian Paediatric Surveillance Unit (APSU) over a 10-month period and an estimated 256 cases of intussusception expected in Australian infants per year.[34] The cases reported to ADRAC equate to a rate of 2.7 per 100,000 doses of rotavirus vaccine, similar to the passive reporting rate of intussusception in the US VAERS of 2.3 per 100,000 administered doses, and the active reporting rate of intussusception in the US Vaccine Safety Datalink system of 2.7 per 100,000 doses.[35]

The rotavirus vaccines used in Australia (RotaTeq® and Rotarix®) underwent extensive pre-licensure clinical trials. RotaTeq® was tested in a large phase III trial in 11 countries and included more than 70,000 children. The risk of intussusception was evaluated for 42 days after each vaccine dose and the data didn't suggest any increased risk of intussusception in vaccine recipients relative to that for placebo.[36] Rotarix® was also tested in a large-scale trial of more than 63,000 infants enrolled in 11 Latin American countries and confirmed that during a 31-day period after each dose, there was no increase in intussusception among recipients of vaccine compared with placebo.[37] The major reason for these larger than usual clinical trials related to an association between intussusception within 21 days of receipt of a previously licensed rotavirus vaccine, RotaShield, which was licensed in the USA in 1998 and withdrawn soon afterwards.[38,39] In Australia, ongoing studies on rotavirus vaccine and intussusception are being conducted through the APSU and Paediatric Active Enhanced Disease Surveillance project.

The increase in the AEFI reporting rate for quadrivalent DTPa-IPV for children aged < 1 year was conjointly related to the implementation of the rotavirus vaccine in July 2007 and the changed surveillance practices in Victoria as both the vaccines are co-administered at 2, 4 and 6 months of age. The

increase in children aged 2 to < 7 years was mainly due to reporting of ISR and allergic reactions. ISR were predominantly higher among children aged 2 to < 7 years following the 4th dose of DTPa-IPV and 2nd dose of MMR. This increase was almost entirely due to an increase from Victoria. This AEFI, including extensive limb swelling, is known to be very common among children receiving a 4th and 5th dose of acellular pertussis-containing vaccine,[15,17,19,21] while the concomitantly administered MMR is likely to be included in these reports. It has been reported that 10% of children experience erythema > 5 cm with any pertussis containing vaccine including DTPa_IPV.[34] The reporting rate of ISR in this age group appeared to decline in recent years, as was expected following the removal of the dose due at 18 months of age from the NIP in September 2003. Children entering school in 2008 would have received their 4th dose of an acellular pertussis-containing vaccine at 4–5 years of age, whereas children in earlier birth cohorts would have received their 5th dose prior to school entry. It is likely that there is less under-reporting of ISR in Victoria and more in other jurisdictions, and that the incidence of this adverse event is higher than previously documented. There was a substantial decrease (497 records in 2008 compared with 705 records in 2007) in reports for HPV vaccine during 2008 and most were mild events that had been identified in pre-licensure clinical trials.[32,33] These included mainly milder allergic reactions and injection site reactions. A range of mild non-specific symptoms including headache, nausea, dizziness, malaise and weakness were also commonly reported (Table 6).[40,41]

Conclusion

AEFI reports in 2008 showed a decrease in reports in adolescents during the second year of the national HPV program, an increase in reports in children associated with a continued high rate of reports associated with rotavirus vaccines, and increases in children and adults associated with improved sensitivity of surveillance in Victoria. The majority of AEFI reports were of mild, transient and well-recognised vaccine side-effects. When compared with the illness prevented by these vaccines, this report demonstrates again that the benefits of immunisation outweigh the risks.

While under-reporting is a known disadvantage of passive surveillance systems, the Australian national AEFI passive surveillance system is sufficiently sensitive to detect expected changes in AEFI reporting associated with changes in immunisation programs. Processes are in place to investigate signals and monitor trends in AEFI reporting.[31,40] The regular analysis and publication of national AEFI surveillance data collated in the ADRAC database remains an important aspect of Australia's immunisation program.

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Abbreviations of vaccine types

7vPCV	7-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 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
Hib-HepB	combined *Haemophilus influenzae* type b and hepatitis B
HPV	human papillomavirus
IPV	inactivated poliovirus vaccine
Men4PV	meningococcal polysaccharide tetravalent vaccine
MenCCV	meningococcal C conjugate vaccine
MMR	measles-mumps-rubella