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## **Surveillance of adverse events following immunisation in Australia: annual report, 2018**

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# Surveillance of adverse events following immunisation in Australia: annual report, 2018

Aditi Dey, Han Wang, Helen Quinn, Alexis Pillsbury, Catherine Glover, Megan Hickie, Nicholas Wood, Frank Beard and Kristine Macartney

## Abstract

This report summarises Australian spontaneous surveillance data for adverse events following immunisation (AEFI) for 2018 reported to the Therapeutic Goods Administration and describes reporting trends over the 19-year period 1 January 2000 to 31 December 2018. There were 4221 AEFI records for vaccines administered in 2018, an annual AEFI reporting rate of 16.9 per 100,000 population. There was a 2.9% increase in the overall AEFI reporting rate in 2018 compared to 2017. This slight increase in reported adverse events in 2018 was likely due to new additions to the National Immunisation Program schedule, namely meningococcal ACWY vaccination for children aged 12 months, enhanced immunogenicity trivalent influenza vaccines for adults aged  $\geq 65$  years, and state- and territory-funded seasonal influenza vaccination programs for children aged 6 months to  $< 5$  years. AEFI reporting rates for most individual vaccines in 2018 were similar to 2017. The most commonly reported adverse events were injection site reaction (34%), pyrexia (15%), rash (15%), vomiting (8%), headache (6%) and pain (6%). Two deaths were reported to the TGA but no clear causal relationship with vaccination was found.

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

## Introduction

This report summarises national spontaneous surveillance data for adverse events following immunisation (AEFI) reported to the Therapeutic Goods Administration (TGA). The report focuses on AEFI reported for vaccines administered during 2018 and on trends in AEFI reporting over the 19-year period 1 January 2000 – 31 December 2018.

An adverse event following immunisation is defined as any untoward medical occurrence which follows immunisation and which does not necessarily have a causal relationship with the usage of the vaccine.<sup>1</sup> The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.<sup>1</sup> Thus, AEFI may be caused by a vaccine(s) or may be coincidental. Adverse events may also include conditions that occur following the incorrect handling and/or administration of a vaccine(s). The post-marketing surveillance of AEFI is particularly important to detect signals of rare, late onset or unexpected events, which are difficult to detect in pre-registration vaccine trials.

Reports summarising national AEFI surveillance data have been published regularly since 2003.<sup>2–15</sup> Trends in reported AEFI are influenced by changes to vaccine funding and availability through the National Immunisation Program (NIP), and the impact of these changes on the interpretation of trend data has been described in previous reports published since 2003.<sup>2–15</sup> Changes to the NIP since 2005 are summarised in Table 1. Recent changes that impact on AEFI surveillance data presented in this 2018 report are:

- October 2018
  - Multicomponent recombinant meningococcal B vaccine funded by SA for children 6 weeks to 12 months of age, with catch-up for children from 12 months to <4 years of age
- July 2018
  - Meningococcal ACWY conjugate vaccine funded for all children at 12 months of age, replacing combined Hib and meningococcal C-containing vaccine
  - Hib dose moved to 18 months and given as monovalent Hib vaccine
  - Schedule for routine childhood vaccination with 13vPCV changed from 2, 4 and 6 months of age to 2, 4 and 12 months of age
- April 2018
  - Enhanced trivalent influenza vaccines (high-dose and adjuvanted) funded nationally for all adults aged ≥65 years
  - Annual seasonal influenza vaccination funded by ACT, NSW, Qld, SA, TAS and Vic for all children aged 6 months to <5 years
  - Meningococcal A, C, Y, W-135 conjugate vaccine funded by SA for Aboriginal and Torres Strait Islander children and adolescents aged 12 months to 19 years living in the Eyre and Far North, and Flinders and Upper North regions
- February 2018
  - Meningococcal A, C, Y, W-135 conjugate vaccine funded by ACT for grade 10 students and persons aged 16–19 years who no longer attend school
- A 2-dose schedule of 9vHPV funded for adolescents aged 12–14 years, delivered through a school-based program; 4vHPV ceased to be used in the program
- January 2018
  - Meningococcal A, C, Y, W-135 conjugate vaccine funded by WA for children aged 12 months to <5 years
  - Meningococcal ACWY school-based vaccination program funded for all NSW secondary school students in Years 10 and 11, as well as adolescents aged 15 to 19 years who have not received the vaccine at school.

To assist readers, at the end of this report there is a glossary of the abbreviations of the vaccines referred to in this report.

## Methods

AEFI are notified to the TGA by state and territory health departments, health professionals, vaccine companies and members of the public.<sup>16</sup> All reported AEFI are assessed using internationally consistent criteria<sup>17</sup> and entered into the Australian Adverse Events Management System (AEMS) database. Where there is insufficient information to determine causality for select serious adverse events the TGA will attempt to contact the reporter on up to three occasions to elicit further information. Data mining and signal detection activities are also conducted by the TGA.

## AEFI data

De-identified information on all AEFI reported to the TGA from 1 January 2000 to 31 December 2018 and stored in the AEMS database were released to the National Centre for Immunisation Research and Surveillance (NCIRS) in July 2019. Readers are referred to previous AEFI surveillance reports for a description of the surveillance system.<sup>3,6</sup>

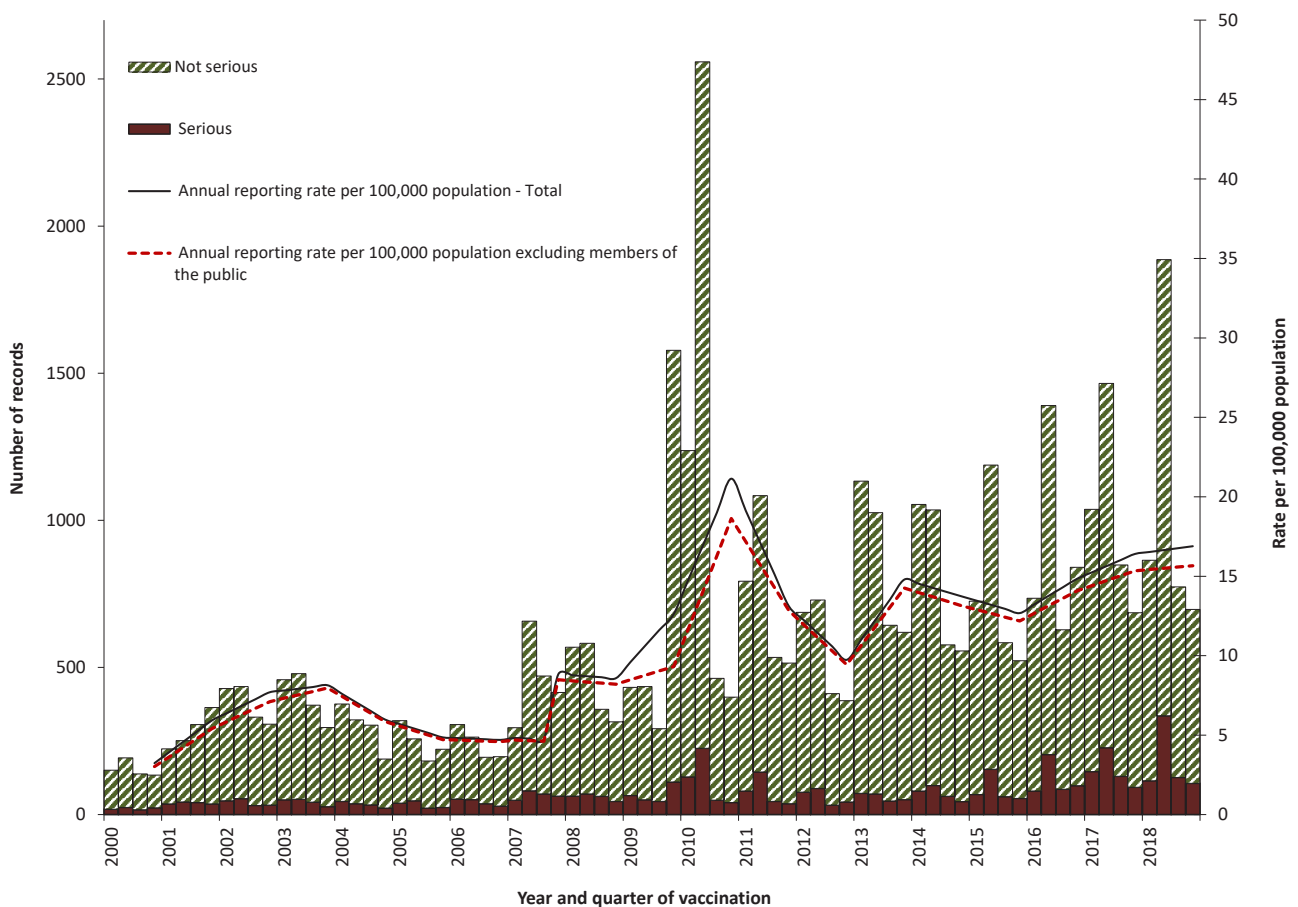
**Table 1: Changes in immunisation policy and the National Immunisation Program (2005–2018)**<sup>2,4,5,7,10,12,14,15,36,37,40</sup>

Year	Change
2018	<p><b>October 2018</b></p> <ul style="list-style-type: none"> <li>Multicomponent recombinant meningococcal B vaccine funded by SA for children 6 weeks to 12 months of age, with catch-up for children from 12 months to &lt;4 years of age</li> </ul> <p><b>July 2018</b></p> <ul style="list-style-type: none"> <li>Meningococcal ACWY conjugate vaccine funded for all children at 12 months of age, replacing combined Hib and meningococcal C-containing vaccine</li> <li>Hib dose moved to 18 months and given as monovalent Hib vaccine.</li> <li>Schedule for routine childhood vaccination with 13vPCV changed from 2, 4 and 6 months of age to 2, 4 and 12 months of age.</li> </ul> <p><b>April 2018</b></p> <ul style="list-style-type: none"> <li>Enhanced trivalent influenza vaccines (high-dose and adjuvanted) funded nationally for all adults aged ≥65 years.</li> <li>Annual seasonal influenza vaccination funded by ACT, NSW, Qld, SA, TAS and Vic for all children aged 6 months to &lt;5 years</li> <li>Meningococcal A, C, Y, W-135 conjugate vaccine funded by SA for Aboriginal and Torres Strait Islander children and adolescents aged 12 months to 19 years living in the Eyre and Far North, and Flinders and Upper North regions</li> </ul> <p><b>February 2018</b></p> <ul style="list-style-type: none"> <li>Meningococcal A, C, Y, W-135 conjugate vaccine funded by ACT for grade 10 students and persons aged 16–19 years who no longer attend school</li> <li>A 2-dose schedule of 9vHPV funded for adolescents aged 12–14 years, delivered through a school-based program; 4vHPV ceased to be used in the program.</li> </ul> <p><b>January 2018</b></p> <ul style="list-style-type: none"> <li>Meningococcal A, C, Y, W-135 conjugate vaccine funded by WA for children aged 12 months to &lt;5 years</li> <li>Meningococcal ACWY school-based vaccination program funded for all NSW secondary school students in Years 10 and 11, as well as adolescents aged 15 to 19 years who have not received the vaccine at school.</li> </ul>
2017	<p>From January to December 2017, meningococcal ACWY conjugate vaccine funded in Western Australia, Victoria and Tasmania for grade 10–12 students; New South Wales for grade 11–12; Queensland grade 10 students and persons aged 15–19 years who no longer attend school. The Northern Territory introduced the vaccine for at-risk people aged 1–19 years living in specified remote regions and all children aged 12 months. For more details see the meningococcal vaccination history table at <a href="http://ncirs.org.au/sites/default/files/2019-04/Meningococcal-history-April-2019.pdf">http://ncirs.org.au/sites/default/files/2019-04/Meningococcal-history-April-2019.pdf</a></p> <p>From April 2017, meningococcal B vaccine study commenced in South Australia for grade 10–12 students at participating schools.</p>
2016	<p>From November 2016, zoster vaccine (Zostavax®) provided free for people aged 70 years under the National Immunisation Program (NIP) with a five year catch-up program for people aged 71–79 years.</p> <p>From March 2016, free booster dose of the diphtheria, tetanus, and acellular pertussis-containing vaccine (DTPa) at 18 months of age.</p>
2015	<p>From March 2015, seasonal influenza vaccine funded for Aboriginal and Torres Strait Islander children aged 6 months to less than 5 years.</p> <p>From March to June 2015, the dTpa vaccine for women during the third trimester of pregnancy was funded by New South Wales, South Australia, Western Australia, the Australian Capital Territory, Victoria and Tasmania. The Northern Territory had funded it since September 2013 and Queensland since July 2014.</p> <p>In March 2015, a booster dose of DTPa vaccine recommended at 18 months of age (funded in March 2016).</p> <p>In April 2015, new immunisation requirements for family assistance payments were announced by the federal government (the ‘No Jab, No Pay’ policy), to come into effect on 1 January 2016. Only parents of children (aged less than 20 years) who are ‘fully immunised’ or on a recognised catch-up schedule remain eligible to receive the Child Care Benefit, Child Care Rebate, and/or the Family Tax Benefit Part A end-of-year supplement.</p>

Year	Change
2014	4vHPV vaccine catch-up program for males aged 14–15 years ceased in December 2014. In July 2014, dTpa vaccine was funded by Queensland for women during the third trimester of pregnancy.
2013	From 1 February 2013, 4vHPV vaccine was extended to males aged 12–13 years, delivered through a school-based program, with a catch-up program for males aged 14–15 years in 2013 and 2014. From July 2013, the second dose of MMR vaccine, previously given at 4 years, was brought forward to 18 months of age and delivered as MMRV vaccine. From July 2013, combined <i>Haemophilus influenzae</i> type b (Hib) and meningococcal serogroup C (MenC) vaccine, Menitorix®, was funded for infants aged 12 months. This combination vaccine replaced the single dose of monovalent meningococcal C conjugate vaccine (MenCCV) and booster dose of monovalent Hib vaccine previously scheduled at 12 months of age. At the end of December 2013, the secondary school Year 7 hepatitis B vaccine catch-up program ceased, as all younger age cohorts were eligible for infant immunisation under the NIP (commenced 2000). In September 2013, dTpa vaccine funded by NT for women during the third trimester of pregnancy and for parents of infants aged <7 months under cocoon strategy
2012	From 1 October 2012, a fourth dose of Prevenar 13®, (13vPCV, a 13-valent pneumococcal conjugate vaccine) was listed on the National Immunisation Program (NIP) for Indigenous children, aged 12–18 months, residing in Queensland, South Australia, Western Australia and the Northern Territory. This replaced the booster dose of Pneumovax®23, (23vPPV, a 23-valent pneumococcal polysaccharide vaccine) administered between 18 and 24 months of age for Indigenous children from these jurisdictions.
2011	From 1 July 2011, Prevenar 13® replaced Prevenar® on the NIP for children at 2, 4 and 6 months of age in all states and territories except the Northern Territory which adopted 13vPCV from 1 October 2011. 1 October 2011 to 30 September 2012: all children aged between 12 - 35 months who had completed a primary pneumococcal vaccination course with 7vPCV were eligible to receive a free supplementary dose of Prevenar 13®. On 25 March 2011, TGA issued a recall of Batch N3336 of the 23 valent pneumococcal polysaccharide vaccine 23vPPV, Pneumovax®23. April 2011: health professionals were advised not to administer a second or subsequent dose of Pneumovax®23 vaccine. December 2011: Revised recommendations regarding which patients should be re-vaccinated under the NIP were provided.
2010	Annual vaccination with seasonal trivalent influenza vaccine (TIV, containing 3 influenza strains: A/H1N1, A/H3N2 and B) was funded under the NIP for people aged ≥6 months with medical risk factors (previously subsidised through the Pharmaceutical Benefits Scheme) and all Indigenous people aged ≥15 years (previously all Indigenous adults ≥50 years and 15–49 years with medical risk factors). On 23 April 2010, the use of the 2010 seasonal TIV in children <5 years of age was suspended by Australia's Chief Medical Officer due to an increased number of reports of fever and febrile convulsions post vaccination. A subsequent investigation identified that Fluvax® and Fluvax® junior (CSL Biotherapies), but neither of the other two available brands registered for use in young children, were associated with an unacceptably high risk of febrile convulsions. The recommendation to resume the use of seasonal influenza vaccine in children aged 6 months to 5 years, using brands other than Fluvax® and Fluvax® junior, was made in August 2010.
2009	By late 2009, all states and territories were using the single hexavalent DTPa-IPV-Hib-HepB (Infanrix® hexa) vaccine for all children at 2, 4 and 6 months of age, due to an international shortage of <i>Haemophilus influenzae</i> type b (Hib) (PedvaxHib® [monovalent] and Comvax® [Hib-HepB]) vaccines. Pandemic H1N1 2009 influenza vaccine (Panvax®) was rolled out across Australia from 30 September 2009 for people aged ≥10 years. From December 2009, the pandemic vaccine was made available to children aged 6 months to 10 years.
2008	Western Australia commenced a seasonal influenza vaccination program for all children aged 6 months to <5 years (born after 1 April 2003). In March 2008, Queensland, South Australia and Victoria changed from using two combination vaccines (quadrivalent DTPa-IPV and Hib-HepB) to the single hexavalent DTPa-IPV-HepB-Hib vaccine.

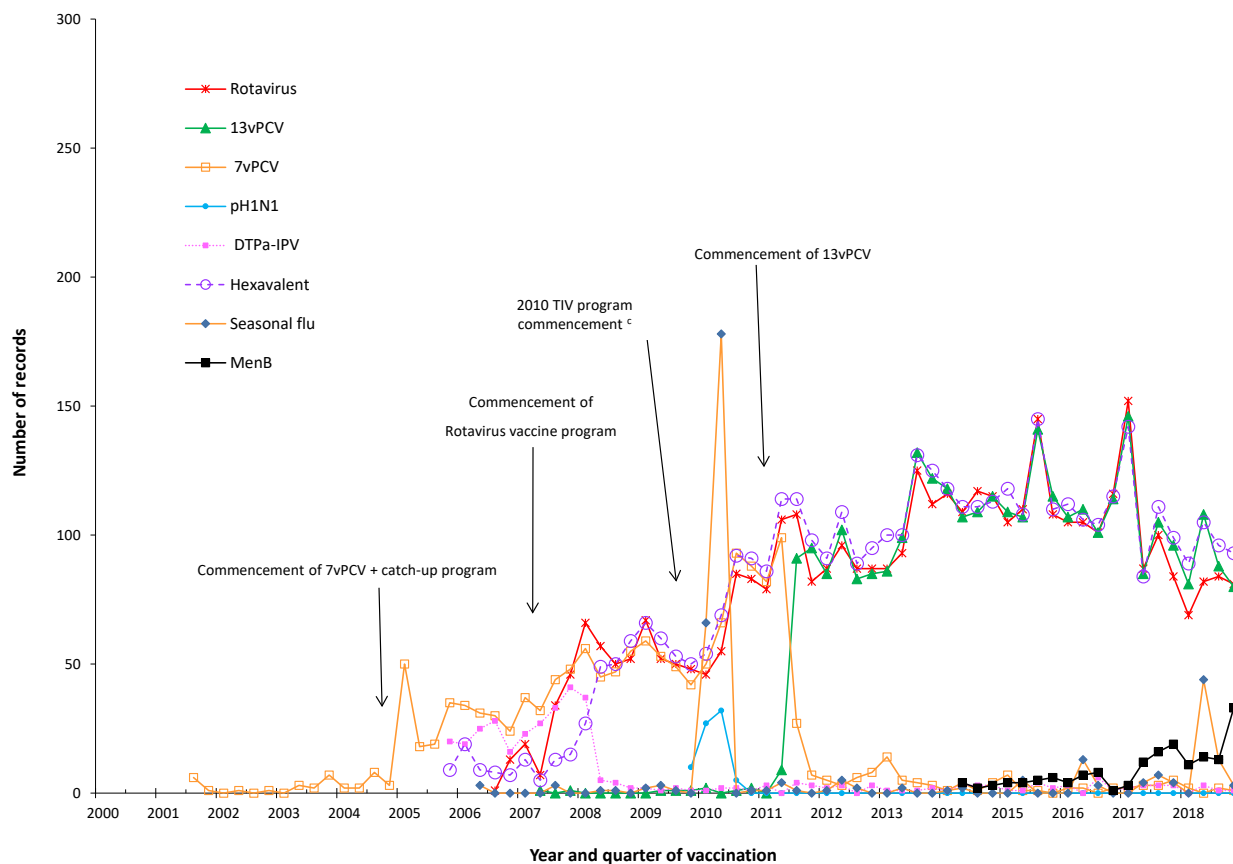
Year	Change
2007	<p>From April 2007, funded immunisation against human papillomavirus for all Australian girls aged 12–13 years delivered through a school-based program from April 2007, with a temporary catch-up program through schools or primary care providers for females aged 13–26 years until December 2009.</p> <p>From July 2007, universal funded immunisation against rotavirus at 2 and 4 months of age (Rotarix®) or at 2, 4 and 6 months of age (Rotateq®).</p>
2005	<p>From January 2005, universal funded infant 7-valent pneumococcal conjugate vaccine (7vPCV) program replaced the previous targeted childhood program, with a catch-up program for children aged &lt;2 years.</p> <p>Universal 23-valent pneumococcal polysaccharide vaccine (23vPPV) for adults aged ≥65 years replaced previous subsidy through the Pharmaceutical Benefits Scheme.</p> <p>From November 2005, universal funded immunisation against varicella at 18 months of age with a school-based catch-up program for children at 10–13 years of age not previously vaccinated and without a history of varicella infection (no funded catch-up for children 2–10 years of age).</p> <p>IPV was funded to replace OPV, in combination vaccines.</p>

**Figure 1: Adverse events following immunisation, AEMS database, 2000 to 2018, by year and quarter of vaccination<sup>a</sup>**



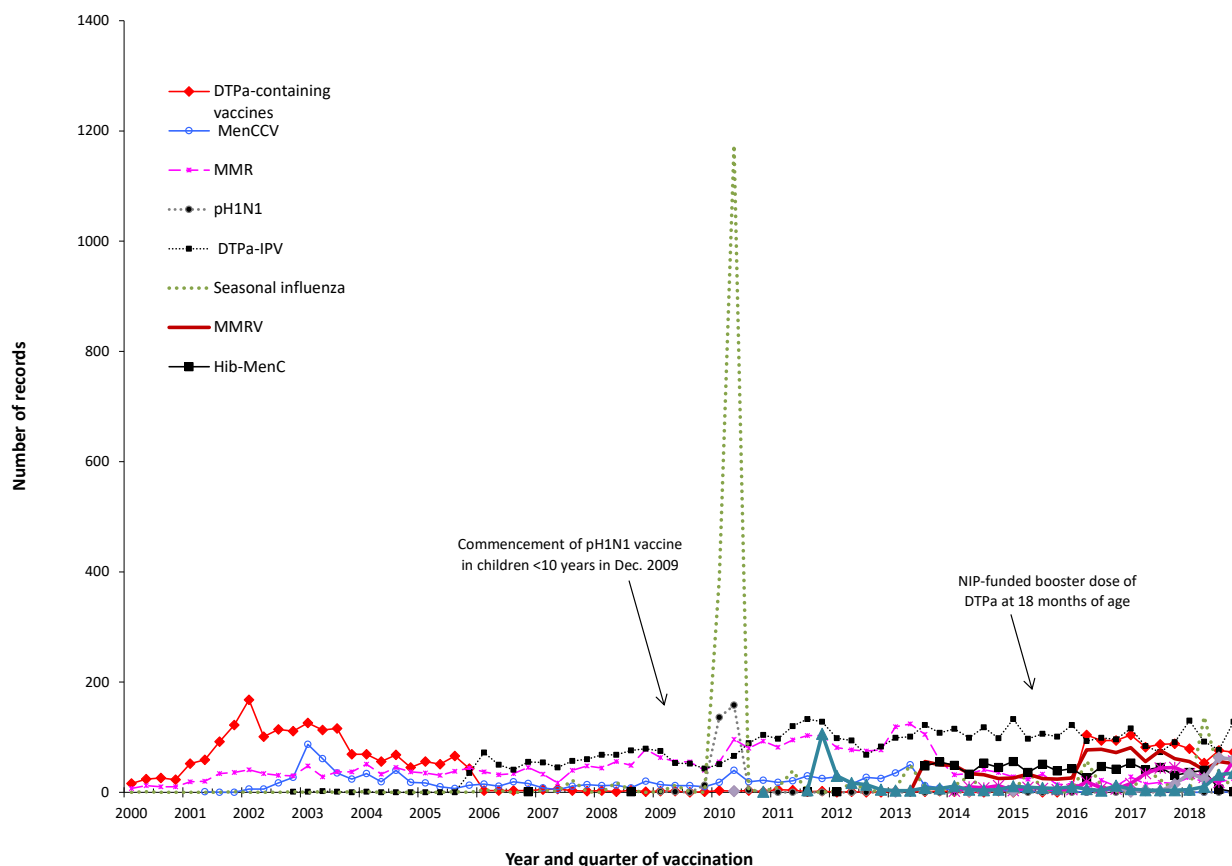
<sup>a</sup> For reports where the date of vaccination was not recorded, the date of onset or date event was reported to TGA was used as a proxy for vaccination date.

**Figure 2: Adverse events following immunisation for children aged <1 year, AEMS database, 2000 to 2018, by year and quarter of vaccination<sup>a,b</sup>**



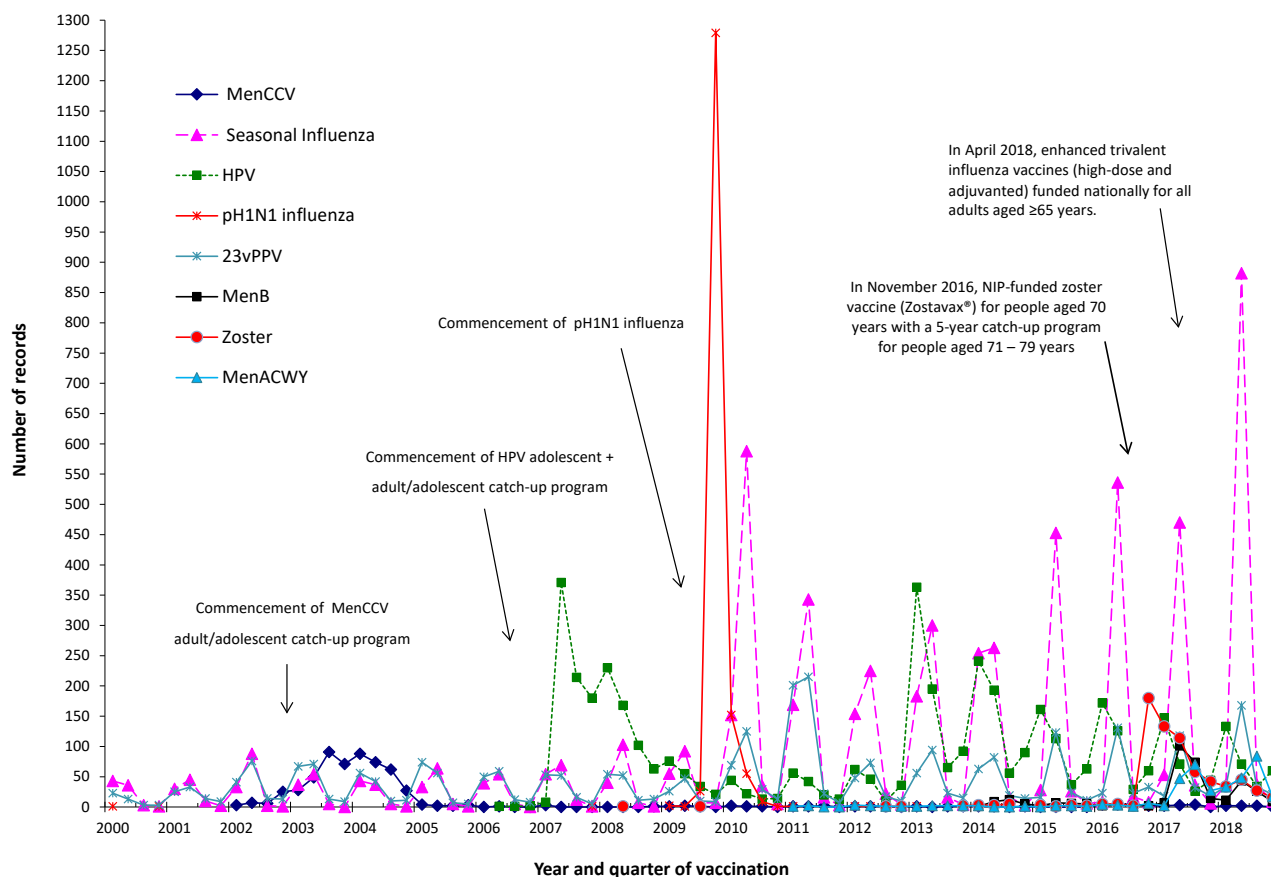
- a For reports where the date of vaccination was not recorded, the date of onset or date event was reported to TGA was used as a proxy for vaccination date.
- b DTPa-IPV and DTPa-IPV-HepB-Hib (hexavalent) vaccines were introduced into the NIP schedule in November 2005; rotavirus (Rotateq<sup>®</sup> and Rotarix<sup>®</sup>) vaccines on 1 July 2007; pH1N1 influenza vaccine for children 6 months to 10 years on December 2009; seasonal trivalent influenza vaccine in 2010 which was an extension of existing adult and Indigenous programs to at risk populations; and the 13-valent pneumococcal conjugate vaccine (13vPCV) on 1 July 2011. In July 2018, the schedule for routine childhood vaccination with 13vPCV changed from 2, 4 and 6 months of age to 2, 4 and 12 months of age. Also, MenB vaccine is recommended for use in those with increased risk of invasive meningococcal disease and is not currently funded under the NIP. In October 2018, a multicomponent recombinant meningococcal B vaccine was funded by SA for children 6 weeks to 12 months of age, with catch-up for children from 12 months to <4 years of age.
- c Safety signal for fever and febrile convulsion found to be due to Seqirus (formerly bioCSL) Fluvax<sup>®</sup> 2010 TIV in children

Figure 3: Adverse events following immunisation for children aged 1 to <7 years in frequently reported vaccines, AEMS database, 2000 to 2018, by year and quarter of vaccination<sup>a,b</sup>



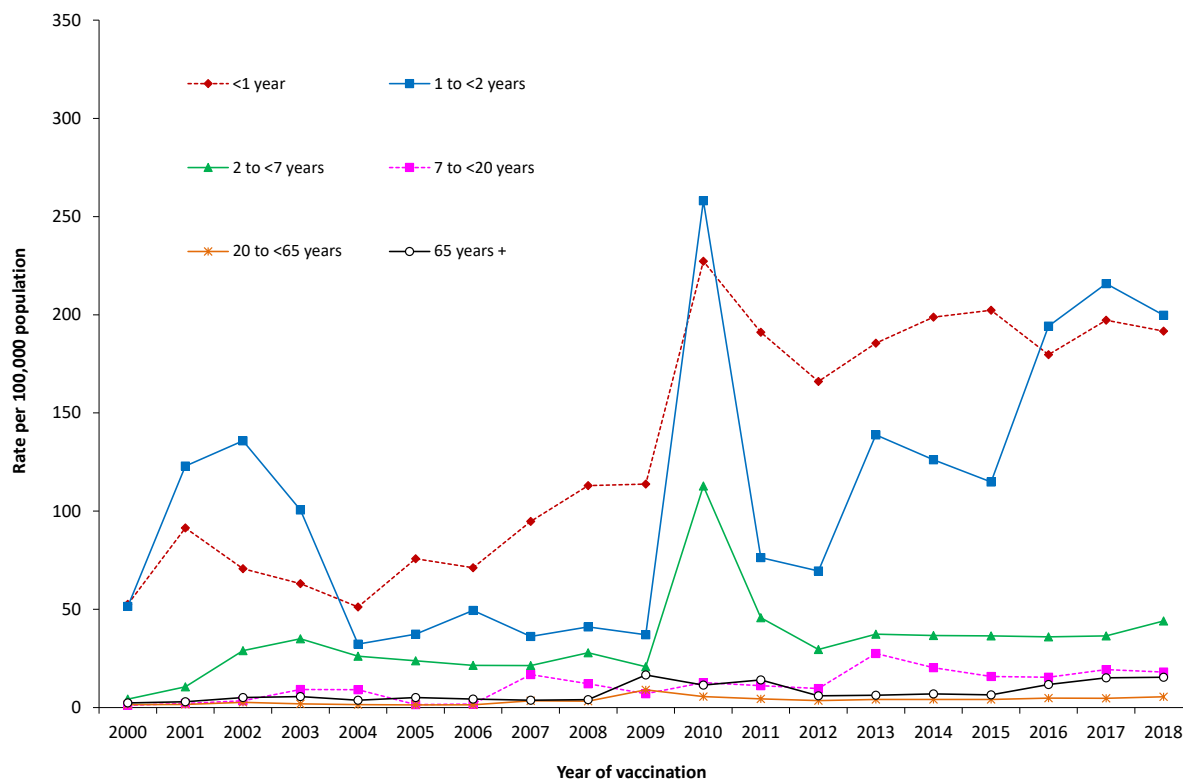
- a For reports where the date of vaccination was not recorded, the date of onset or date event was reported to TGA was used as a proxy for vaccination date.
- b DTPa-IPV vaccine was introduced into the NIP schedule in November 2005 replacing DTPa and OPV vaccines; seasonal trivalent influenza vaccine in 2010 which was an extension of existing adult and Indigenous programs to at risk populations; MMRV and Hib–MenC vaccines on July 2013, and HPV vaccine program extended to boys in February 2013. MenB vaccine is recommended for use in those with increased risk of invasive meningococcal disease and is not currently funded under the NIP. In April 2016, NIP-funded booster dose of DTPa vaccine was introduced at 18 months of age. In October 2018, a multicomponent recombinant meningococcal B vaccine was funded by SA for children 6 weeks to 12 months of age, with catch-up for children from 12 months to <4 years of age. In July 2018, a meningococcal ACWY conjugate vaccine funded for all children at 12 months of age, replacing combined Hib and meningococcal C-containing vaccine. The Hib dose was moved to 18 months and given as a monovalent Hib vaccine.

**Figure 4. Adverse events following immunisation for people aged  $\geq 7$  years in frequently reported vaccines, AEMS database, 2000–2018, by year and quarter of vaccination.<sup>a,b</sup>**



- a For reports where the date of vaccination was not recorded, the date of onset or date event was reported to TGA was used as a proxy for vaccination date.
- b MenCCV was introduced into the NIP schedule on 1 January 2003; pH1N1 influenza vaccine for children 6 months to 10 years on December 2009; pH1N1 vaccination for those  $\geq 10$  years commenced on 30 September 2009; seasonal trivalent influenza vaccine in 2010 which was an extension of existing adult and Indigenous programs to at risk populations; and HPV vaccine program extended to boys in February 2013. MenB vaccine is recommended for use in those with increased risk of invasive meningococcal disease and is not currently funded under the NIP.
- In November 2016, zoster vaccine (Zostavax<sup>®</sup>) was NIP-funded for people aged 70 years with a 5-year catch-up program for people aged 71–79 years.
- In April 2018, enhanced trivalent influenza vaccines (high-dose and adjuvanted) funded nationally for all adults aged  $\geq 65$  years.

Figure 5: Reporting rates of adverse events following immunisation per 100,000 population, AEMS database, 2000 to 2018, by age group and year of vaccination<sup>a</sup>



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

Records<sup>i</sup> contained in the AEMS database were eligible for inclusion in the analysis if a vaccine was recorded as ‘suspected’<sup>ii</sup> of causal involvement in the reported adverse event and *either*

- The vaccination occurred between 1 January 2000 and 31 December 2018, or
- 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 2018.

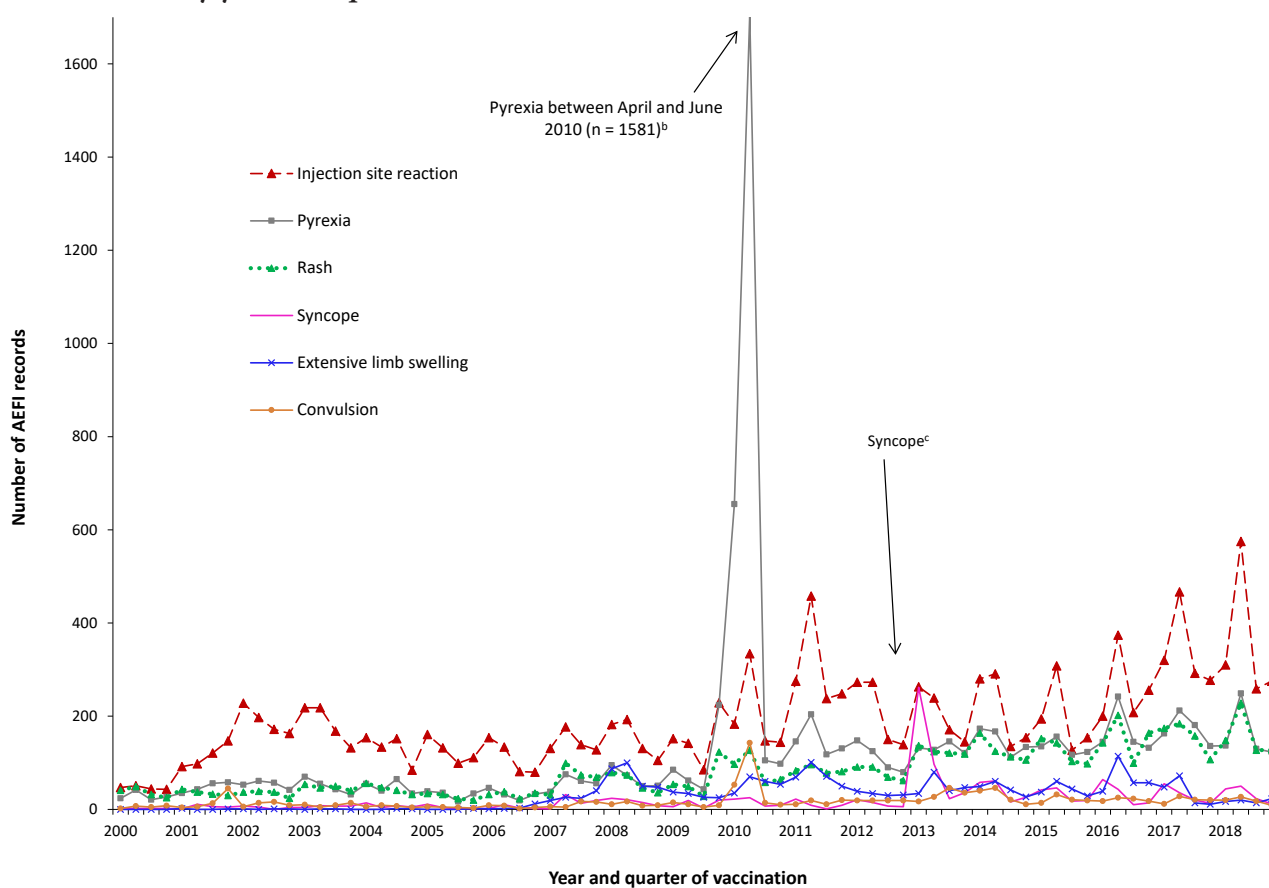
i The term ‘AEFI record’ is used throughout this report because a single AEFI notification/report to the TGA can generate more than one record in the AEMS database. This may occur if there is a time sequence of separate adverse events in a single patient, such as local and systemic adverse events.

ii 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.

## Study definitions of AEFI outcomes

Australian sponsors are required to apply seriousness coding to vaccine AEFI reports to ensure legislated requirements are met. Reports are coded as ‘serious’ or ‘non-serious’ based on criteria similar to those used by the World Health Organization<sup>17</sup> and the US Vaccine Adverse Events Reporting System.<sup>18</sup> An adverse event report is defined as ‘serious’ if it meets one or more of the following criteria: (1) results in death; (2) is life-threatening; (3) requires inpatient hospitalisation or prolongation of existing hospitalisation; (4) results in persistent or significant disability/incapacity; (5) is a congenital anomaly/birth defect; or (6) is a medically important event or reaction. Typically, each AEFI record lists several reaction terms that are symptoms, signs and/or diagnoses that have been coded by TGA staff from the reporter’s description into standardised terms using the Medical Dictionary for Regulatory Activities (MedDRA).<sup>19,20</sup>

Figure 6: Selected frequently reported adverse events following immunisation, AEMS database, 2000 to 2018, by year and quarter of vaccination<sup>a</sup>



- a For reports where the date of vaccination was not recorded, the date of onset or date event was reported to TGA was used as a proxy for vaccination date.
- b Associated with administration of Seqirus (formerly bioCSL) Fluvax® 2010 TIV and associated stimulated reporting.
- c The peak in syncope coincided with the enhanced HPV surveillance program in which there was stimulated reporting of syncope for the first 6 months of 2013.

A limitation of our report was interpretation of the ‘serious’ code for reported adverse events which, while included for completeness, is primarily used as a guide for sponsor reporting. As it is not necessarily applied based on review of detailed and verified clinical data, and may not capture all medically important events, reporting rates of serious adverse events are unlikely to be robust.

In reports published previously, in order to analyse the data, MedDRA coding terms were grouped to create a set of reaction categories that were broadly analogous to the adverse events listed in previous editions of the *Australian Immunisation Handbook*.<sup>16,21</sup> However, the methodological framework of reporting of adverse

events was revised in 2014 and an amended format for AEFI analyses using MedDRA preferred terms (PTs) was adopted.<sup>22</sup> Since 2014, MedDRA PTs have been used for analysis in our reports. Grouping of adverse events using PTs is more comparable with data from other countries and internationally accepted.<sup>23–25</sup> In conjunction with the currently used national vaccine-specific reporting form,<sup>26</sup> the use of PTs allows better reflection of post-marketing surveillance data on vaccines in Australia.

### Data analysis

All data analyses were performed using SAS software version 9.4.<sup>27</sup> Average annual population-based AEFI reporting rates were calculated

for each state and territory and by age group, using 2018 population estimates obtained from the Australian Bureau of Statistics.<sup>28</sup> All rates are presented as average annual rates per 100,000 population. AEFI reporting rates per 100,000 administered doses were estimated where information was available on the number of doses administered. The number of administered doses of each of the vaccines given was obtained from the Australian Immunisation Register (AIR), a national population-based register.<sup>29</sup> From 30 September 2016, the Australian Childhood Immunisation Register (ACIR) became a whole-of-life register (AIR), with the ability to record all vaccinations for people of all ages given by a registered vaccination provider.<sup>30</sup> As part of the transition to a whole-of-life register, from late 2018, all vaccinations given through school-based programs should be recorded on the AIR.

### Notes on interpretation

Caution is required when interpreting the data presented in this report. Due to reporting delays and late onset of some AEFI, the data are considered preliminary, particularly for the fourth quarter of 2018. Data published in previous reports may differ from those presented in this report for the same period because this report has been updated to include delayed notifications to the TGA that were not included in previous publications. Data can also differ because records may be updated and recoded when follow-up information is received or when vaccine-specific analyses are conducted.

The information collated in the AEMS database is intended primarily for signal detection and hypothesis generation. While AEFI reporting rates can be estimated using appropriate denominators, they cannot be interpreted as incidence rates due to under-reporting and biased reporting of suspected events, and the variable quality and completeness of information provided in individual notifications.<sup>3-14,31</sup>

It is important to note that this report is based on vaccine information and MedDRA PTs collated in the AEMS database and not on

comprehensive clinical notes or case reviews. The reported symptoms, signs and diagnoses in each AEFI record in the AEMS database are temporally associated with vaccination but are not necessarily causally associated with a vaccine or vaccines.

For children aged 7 years to <17 years, AEFI reporting rates for HPV, dTpa booster and meningococcal ACWY vaccines should be interpreted with caution due to possible under-reporting/transitioning issues of school-based vaccinations to the AIR.

### Comparison with online Database of Adverse Events Notifications (DAEN)

In August 2012, the TGA made available to the public on its website a searchable database, the Database of Adverse Event Notifications (DAEN), that contains reports of adverse event reports for medicines and vaccines.<sup>32</sup> The data in this report have not been downloaded from DAEN. This report uses data sent to NCIRS by the TGA and includes more detailed information than provided by DAEN. The numbers published in this report may be different from the numbers in DAEN, due to different dates of data extraction and amendment to reports where further information has become available. In addition, this report provides several features that are not available from DAEN, including long-term trends and population and dose-based reporting rates, described in the context of changes in vaccine policy and utilisation, and in reporting practices.

### Results

The AEMS database included a total of 4221 records where the date of vaccination (or onset of adverse event, if vaccination date was not reported) was between 1 January and 31 December 2018. Of these, 56.4% (2380) were in females, 41.8% (1763) in males and 1.8% (78) missing data on sex. Also, 1.5 % (62) were reported in Aboriginal and Torres Strait Islander people.

Table 2: Vaccine types listed as 'suspected' in records of adverse events following immunisation by age groups (<7, 7–17, 18–64 and ≥65 years), AEMS database, 2018

Vaccines <sup>a</sup>	AEFI records <sup>b</sup> (n)	Vaccine Doses <sup>c</sup> 2018	Reporting rate <sup>d</sup> per 100,000 doses (95% CI)	
			2018	2017
<b>&lt;7 years</b>				
DTPa-containing vaccines	1,127	1,451,925	77.6 (73.2 – 82.3)	79.5 (75.0 – 84.2)
• Hexavalent (DTPa-IPV- HepB-Hib)	411	850,171	48.3 (43.8 – 53.2)	50.6 (45.9 – 55.6)
• DTPa-IPV	284	300,527	94.5 (83.8 – 106.1)	117.2 (105.5 – 129.9)
• DTPa	432	301,227	143.4 (130.2 – 157.6)	122.9 (110.7 – 136.0)
Pneumococcal conjugate -13vPCV	439	821,374	53.4 (48.6 – 58.7)	50.5 (45.9 – 55.4)
Rotavirus vaccine	319	547,545	58.3 (52.0 – 65.0)	60.0 (54.3 – 66.1)
Seasonal influenza	240	694,620	34.6 (30.3 – 39.2)	59.3 (47.0 – 73.8)
Measles-mumps-rubella	228	309,005	73.8 (64.5 – 84.0)	70.4 (61.5 – 80.2)
Meningococcal ACWY	211	310,909	67.9 (59.0 – 77.7)	–
Meningococcal B	207	199,745	103.6 (90.0 – 118.7)	120.3 (103.5 – 139.1)
Measles-mumps-rubella-varicella	206	302,682	68.1 (59.1 – 78.0)	87.7 (77.5 – 98.9)
Hib-MenC	91	155,851	58.4 (47.0 – 71.7)	54.6 (46.7 – 63.5)
Varicella	20	16,036	124.7 (76.2 – 192.6)	173.0 (109.7 – 259.6)
<i>Haemophilus influenzae</i> type b	13	16,191	80.3 (42.8 – 137.3)	36.7 (7.6 – 107.2)
Hepatitis B	10	31,066	32.2 (15.4 – 59.2)	25.8 (11.1 – 50.9)
Meningococcal C conjugate	2	5,126	39.0 (4.7 – 140.9)	161.7 (86.1 – 276.5)

Vaccines <sup>a</sup>	AEFI records <sup>b</sup> (n)	Vaccine Doses <sup>c</sup> 2018	Reporting rate <sup>d</sup> per 100,000 doses (95% CI)	
			2018	2017
<b>7–17 years</b>				
HPV	288	500,522	57.5 (51.1 – 64.6)	–
dTpa	219	161,438	135.7 (118.3 – 154.8)	–
Meningococcal ACWY	147	232,731	63.2 (53.4 – 74.2)	–
Seasonal influenza	93	381,689	24.4 (19.7 – 29.8)	–
Meningococcal B	72	54,968	131.0 (102.5 – 164.9)	–
Measles-mumps-rubella	11	25,975	42.3 (21.1 – 75.8)	–
23vPPV	11	2,192	501.8 (250.8 – 896.1)	–
Varicella	8	16,411	48.7 (21.1 – 75.8)	–
dTpa-IPV	7	4,817	145.3 (58.4 – 299.2)	–
Hepatitis B	5	32,089	15.6 (5.1 – 36.4)	–
Meningococcal C conjugate	4	10,294	38.9 (10.6 – 99.5)	–
Measles-mumps-rubella-varicella	2	7,467	26.8 (3.2 – 96.7)	–
<b>18–64 years</b>				
Seasonal influenza	534	1875,459	28.5 (26.1 – 31.0)	–
dTpa	120	454,466	26.4 (21.9 – 31.6)	–
23vPPV	47	41,593	113.0 (83.0 – 150.2)	–
MMR	44	81,888	53.7 (39.0 – 72.1)	–
Hepatitis B	35	136,170	25.7 (17.9 – 35.7)	–
Meningococcal ACWY	34	71,705	47.4 (32.8 – 66.3)	–
Hepatitis A	22	126,839	17.3 (10.9 – 26.3)	–
Meningococcal B	18	22,959	78.4 (46.5 – 123.9)	–
Varicella	13	26,403	49.2 (26.2 – 84.2)	–

Vaccines <sup>a</sup>	AEFI records <sup>b</sup> (n)	Vaccine Doses <sup>c</sup> 2018	Reporting rate <sup>d</sup> per 100,000 doses (95% CI)	
			2018	2017
Hepatitis A-typhoid	11	139,311	7.9 (3.9 – 14.1)	–
Hepatitis A-hepatitis B	9	70,969	12.7 (5.8 – 24.1)	–
Q fever	5	n/a	–	–
<b>≥65 years</b>				
Seasonal influenza	338	2,058,186	16.4 (14.7 – 18.3)	–
23vPPV	198	266,339	74.3 (64.3 – 85.4)	–
Zoster	112	227,092	49.3 (40.6 – 59.3)	–
dTpa	18	79,994	22.5 (13.3 – 35.6)	–

a Records where at least one of the vaccines shown in the table was suspected of causal involvement in the reported adverse event.

b Number of AEFI records in which the vaccine was coded as 'suspected' of causal involvement in the reported adverse event and the vaccination was administered between 1 January and 31 December 2018. More than one vaccine may be coded as 'suspected' if several were administered at the same time.

c Number of vaccine doses recorded on the AIR and administered between 1 January and 31 December 2018.

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

n/a Not applicable

In 2018, approximately 69.3% (n=2926) of AEFI were reported to the TGA via states and territories, while the rest were reported directly to the TGA by nurses (8.2%; n = 346), medical practitioners (7.4%; n = 312), patients/consumers (7.3%; n = 307), vaccine companies (4.4%; n = 186), hospitals (1.6%; n = 68), pharmacists (1.3%; n = 53) and other healthcare professionals (0.5%, n=23).

## Reporting trends

The overall AEFI reporting rate for 2018 was 16.9 per 100,000 population compared with 16.4 per 100,000 in 2017. The highest rate over the 2000–2018 period was observed in 2010 (17.4 per 100,000), predominantly due to reported AEFI in children following vaccination with the pandemic and 2010 seasonal trivalent influenza vaccines.<sup>12</sup>

Most reported events in 2018 (from all reporter types) were recorded as non-serious, similar to previous years (Figure 1).<sup>10,11</sup> Figures 2, 3 and 4 demonstrate marked variations in reporting levels in all age groups associated with changes to the NIP. The increase in reports in 2018 was predominantly associated with NIP funding for meningococcal ACWY conjugate vaccine for all children at 12 months of age; the enhanced immunogenicity trivalent influenza vaccines (high-dose and adjuvanted) for all adults aged ≥65 years; and state- and territory-funded annual seasonal influenza vaccination for all children aged 6 months to <5 years (Figures 3 & 4).

A seasonal pattern of AEFI reporting was apparent in 2018 as in previous years, with the highest number of AEFI notifications for vaccinations administered in the first half of the year (Figure 1). This corresponds to the months when influenza vaccine is given and older Australians may be more likely to be given 23vPPV in conjunction with the influenza vaccine (April to June). Considerably more AEFI reports following influenza vaccination were received in each year from 2010 onwards than in previous (pre-pandemic) years (Figure 4).

## Age distribution

The highest age-specific AEFI reporting rate per 100,000 population occurred in children aged 1 to <2 years, the age group scheduled to receive meningococcal ACWY vaccination at 12 months of age and the booster dose of DTPa at 18 months of age, and to be affected by the change in schedule for 13vPCV from 2, 4 and 6 months of age to 2, 4 and 12 months of age (Figure 5). Compared to 2017, AEFI reporting rates in 2018 remained relatively stable across most age groups; however, there were slight increases observed in children aged 2 to <7 years and in adults aged 20 to <65 years and 65 years and older (Figure 5).

There were overlapping confidence intervals for reporting rates per 100,000 doses for most individual vaccines in 2018 compared to 2017, noting the new additions to the NIP schedule, namely: meningococcal ACWY vaccination for children aged 12 months; enhanced trivalent influenza vaccines (high-dose and adjuvanted) for adults aged ≥65 years; changes in 13vPCV schedule and in state/territory-based seasonal influenza vaccination programs for children 6 months to <5 years (Table 2).

For children <7 years of age, AEFI reporting rates for varicella and MenC vaccines should be interpreted with caution since monovalent versions of these vaccines were replaced by combination vaccines in July 2013 and hence very few doses of monovalent vaccine were recorded in 2018.

## Geographical distribution

Population-based AEFI reporting patterns varied between states and territories during 2018 (Table 3).

## Vaccines

The vaccine most frequently reported as associated with AEFI was seasonal influenza vaccine (1,261 records; 29.9% of 2018 records) followed by 13vPCV (n = 450, 10.7%), DTPa-IPV (n = 446;

**Table 3: Adverse events following immunisation (AEFI) records, AEMS database, January to December 2018, by jurisdiction**

State or territory	AEFI records		Annual reporting rate per 100,000 population <sup>a</sup>			
	n	(%)	'Serious' <sup>b</sup>	Aged <7 years	Overall Rate	(95% Confidence Interval)
Australian Capital Territory	116	(2.7)	5.2	80.1	27.6	(22.8–33.1)
New South Wales	831	(19.7)	2.4	46.1	10.4	(9.7–11.1)
Northern Territory	74	(1.8)	3.2	145.3	29.9	(23.5–37.6)
Queensland	763	(18.1)	1.9	71.2	15.2	(14.2–16.3)
South Australia	320	(7.6)	2.2	98.8	18.4	(16.5–20.6)
Tasmania	178	(4.2)	8.1	128.5	33.7	(28.9–39.0)
Victoria	1,569	(37.2)	3.2	149.6	24.3	(23.1–25.5)
Western Australia	342	(8.1)	2.3	62.8	13.2	(11.8–14.7)
Other <sup>c</sup>	28	(0.7)	na	na	na	–
Total	4,221	(100.0)	2.7	86.4	16.9	(16.4–17.4)

a Average annual rates per 100,000 population calculated using mid-2018 population estimates (Australian Bureau of Statistics).

b AEFI records defined as 'serious' (i.e. recovery with sequelae, hospitalisation, life-threatening or death).

c Records where the jurisdiction in which the adverse event occurred was not reported or was unclear.

Table 4: Vaccine types listed as 'suspected' in records of adverse events following immunisation (AEFI), AEMS database, 2018

Suspected vaccine type <sup>a</sup>	AEFI records		One suspected vaccine only <sup>b</sup>		'Serious' <sup>c</sup>		Age group <sup>d</sup> <7 years		Age group <sup>d</sup> ≥7 years	
	n	(%)	n	(%) <sup>e</sup>	n	(%) <sup>e</sup>	n	(%) <sup>e</sup>	n	(%) <sup>e</sup>
Influenza	1,261	(29.9)	1,065	(91.7)	234	(20.2)	240	(20.7)	965	(83.1)
13vPCV	450	(10.7)	33	(7.3)	97	(21.6)	439	(97.6)	8	(1.8)
DTPa-IPV	446	(10.6)	395	(88.6)	45	(10.1)	432	(96.9)	12	(2.7)
DTPa-IPV-HepB-Hib	426	(10.1)	58	(13.6)	90	(21.1)	411	(96.5)	9	(2.1)
Men ACWY	396	(9.4)	231	(58.3)	51	(12.9)	211	(53.3)	182	(46.0)
dTpa	357	(8.5)	132	(37.0)	27	(7.6)	0	(0.0)	357	(100.0)
Rotavirus	324	(7.7)	46	(14.2)	74	(22.8)	319	(98.5)	2	(0.6)
HPV	307	(7.3)	116	(37.8)	15	(4.9)	0	(0.0)	298	(97.1)
Meningococcal B	301	(7.1)	217	(72.1)	35	(11.6)	207	(68.8)	89	(29.6)
MMR	301	(7.1)	87	(28.9)	45	(15.0)	228	(75.7)	56	(18.6)
DTPa	284	(6.7)	93	(32.7)	29	(10.2)	284	(100.0)	0	(0.0)
23vPPV	270	(6.4)	168	(62.7)	31	(11.5)	12	(3.8)	256	(96.2)
MMRV	211	(5.0)	29	(13.7)	23	(10.9)	206	(97.6)	3	(1.4)
Zoster	135	(3.2)	126	(93.3)	23	(17.0)	0	(0.0)	122	(90.4)
Hib-MenC	92	(2.2)	5	(5.4)	16	(17.4)	91	(98.9)	0	(0.0)
Hepatitis B	58	(1.4)	38	(65.5)	7	(12.1)	10	(17.2)	40	(69.0)
Hepatitis A	49	(1.2)	10	(20.4)	8	(16.3)	20	(40.8)	29	(59.2)
Varicella	41	(1.0)	18	(43.9)	5	(12.2)	20	(48.8)	21	(51.2)
Typhoid	30	(0.7)	5	(16.7)	3	(10.0)	6	(20.0)	24	(80.0)
BCG	23	(0.5)	20	(87.0)	4	(17.4)	18	(78.3)	0	(0.0)

Suspected vaccine type <sup>a</sup>	AEFI records		One suspected vaccine only <sup>b</sup>		'Serious' <sup>c</sup>		Age group <sup>d</sup> <7 years		Age group <sup>d</sup> ≥7 years	
	n	(%)	n	(%) <sup>e</sup>	n	(%) <sup>e</sup>	n	(%) <sup>e</sup>	n	(%) <sup>e</sup>
Hepatitis A-Typhoid	21	(0.5)	11	(52.4)	3	(14.3)	0	(0.0)	19	(90.5)
dT	20	(0.5)	13	(65.0)	1	(5.0)	0	(0.0)	20	(100.0)
Rabies	19	(0.5)	13	(68.4)	4	(21.1)	0	(0.0)	19	(100.0)
Hepatitis A + B	14	(0.3)	38	(271.4)	2	(14.3)	0	(0.0)	13	(92.9)
Hib	13	(0.3)	0	(0.0)	1	(7.7)	13	(100.0)	0	(0.0)
IPV	9	(0.2)	3	(33.3)	0	(0.0)	2	(22.2)	6	(66.7)
MenCCV	8	(0.2)	3	(37.5)	3	(37.5)	2	(25.0)	6	(75.0)
Yellow fever	7	(0.2)	3	(42.9)	2	(28.6)	0	(0.0)	6	(85.7)
Q fever	7	(0.2)	7	(100.0)	2	(28.6)	0	(0.0)	6	(85.7)
Japanese encephalitis	5	(0.1)	2	(40.0)	0	(0.0)	2	(40.0)	6	(120.0)
Tetanus	1	(0.0)	1	(100.0)	0	(0.0)	0	(0.0)	1	(100.0)

a See appendix for abbreviations of vaccine names.

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

c 'Serious' is defined in the Methods section.

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

e Percentages are calculated for the number of AEFI records where the vaccine was suspected of causal involvement in the event

**Table 5: Selected reported adverse events<sup>a</sup> classified by MedDRA Preferred Terms in records of adverse events following immunisation (AEFI), AEMS database, 2018<sup>b</sup>**

MedDRA Preferred Terms (adverse events)	AEFI records		Only adverse event reported <sup>c</sup>		'Serious' <sup>d</sup>		Age group <sup>e</sup>		Age group <sup>e</sup>	
	N	n	n	(%) <sup>f</sup>	n	(%) <sup>f</sup>	<7 years		≥7 years	
							n	(%) <sup>f</sup>	n	(%) <sup>f</sup>
Injection site reaction <sup>g</sup>	1,419	829	108	(58.4)	108	(7.6)	706	(49.8)	689	(48.6)
Pyrexia	639	37	104	(5.8)	104	(16.3)	372	(58.2)	256	(40.1)
Rash <sup>h</sup>	631	278	52	(44.1)	52	(8.2)	395	(62.6)	228	(36.1)
Vomiting	324	45	61	(13.9)	61	(18.8)	189	(58.3)	125	(38.6)
Headache	274	9	44	(3.3)	44	(16.1)	18	(6.6)	223	(81.4)
Pain	240	47	22	(19.6)	22	(9.2)	32	(13.3)	199	(82.9)
Nausea	225	3	41	(1.3)	41	(18.2)	15	(6.7)	203	(90.2)
Urticaria	196	112	24	(57.1)	24	(12.2)	115	(58.7)	76	(38.8)
Dizziness	184	12	20	(6.5)	20	(10.9)	8	(4.3)	170	(92.4)
Malaise	171	12	26	(7.0)	26	(15.2)	18	(10.5)	149	(87.1)
Diarrhoea	164	15	28	(9.1)	28	(17.1)	102	(62.2)	55	(33.5)
Myalgia	133	7	21	(5.3)	21	(15.8)	5	(3.8)	123	(92.5)
Lethargy	131	1	27	(0.8)	27	(20.6)	47	(35.9)	77	(58.8)
Syncope	129	55	15	(42.6)	15	(11.6)	20	(15.5)	106	(82.2)
Irritability	108	5	11	(4.6)	11	(10.2)	101	(93.5)	3	(2.8)
Angioedema	98	11	24	(11.2)	24	(24.5)	31	(31.6)	67	(68.4)
Pallor	92	6	14	(6.5)	14	(15.2)	53	(57.6)	37	(40.2)
Pruritus	82	7	10	(8.5)	10	(12.2)	19	(23.2)	62	(75.6)
Paraesthesia	79	8	17	(10.1)	17	(21.5)	3	(3.8)	74	(93.7)
Erythema	78	12	11	(15.4)	11	(14.1)	39	(50.0)	38	(48.7)

MedDRA Preferred Terms (adverse events)	AEFI records		Only adverse event reported <sup>f</sup>		'Serious' <sup>d</sup>		Age group <sup>e</sup>	
	N	n	n	n	n	n	Age group <sup>e</sup>	
							(%) <sup>f</sup>	(%) <sup>f</sup>
Extensive limb swelling	74	52	27	27	54	19	(73.0)	(25.7)
Fatigue	74	0	10	10	10	62	(13.5)	(83.8)
Convulsions <sup>i</sup>	74	42	38	38	58	14	(78.4)	(18.9)
Abdominal pain	71	1	13	13	26	43	(36.6)	(60.6)
Decreased appetite	70	0	12	12	53	16	(75.7)	(22.9)
Chills	68	2	14	14	8	58	(11.8)	(85.3)
Cough	67	3	14	14	29	37	(43.3)	(55.2)
Hypotonic-hyporesponsive episode	60	42	29	29	59	0	(98.3)	(0.0)
Injected limb mobility decreased	58	5	3	3	8	49	(13.8)	(84.5)
Flushing	56	0	5	5	6	48	(10.7)	85.7
Dyspnoea	53	2	11	11	8	44	(15.1)	(83.0)
Arthralgia	51	4	13	13	2	47	(3.9)	(92.2)
Somnolence	48	3	8	8	29	19	(60.4)	(39.6)
Presyncope	45	29	5	5	19	25	(42.2)	(55.6)
Anaphylactic reaction	40	29	22	22	7	26	(17.5)	(65.0)
Throat irritation	36	2	7	7	3	32	(8.3)	(88.9)
Hyperhidrosis	32	1	6	6	5	26	(15.6)	(81.3)
Hypoaesthesia	32	3	8	8	1	30	(3.1)	(93.8)
Asthenia	32	0	4	4	2	30	(6.3)	(93.8)
Rhinorrhoea	31	0	4	4	17	13	(54.8)	(41.9)
Oropharyngeal pain	26	0	5	5	1	25	(3.8)	(96.2)
Apnoea	26	10	11	11	23	0	(88.5)	(0.0)

MedDRA Preferred Terms (adverse events)	AEFI records		Only adverse event reported <sup>f</sup>		'Serious' <sup>d</sup>		Age group <sup>e</sup>			
	N	n	n	(%) <sup>f</sup>	n	(%) <sup>f</sup>	<7 years			
							n	(%) <sup>f</sup>		
Chest discomfort	25	0	0	(0.0)	4	(16.0)	1	(4.0)	24	(96.0)
Tachycardia	23	1	1	(4.3)	11	(47.8)	7	(30.4)	16	(69.6)
Cold Sweat	22	0	0	(0.0)	1	(4.5)	2	(9.1)	20	90.9
Chest Pain	18	1	1	(5.6)	7	(38.9)	1	(5.6)	17	94.4
Haematochezia	16	7	7	(43.8)	2	(12.5)	16	(100.0)	0	(0.0)
Hypotonia	16	0	0	(0.0)	8	(50.0)	15	(93.8)	1	(6.3)
Guillain-Barre syndrome	14	11	11	(78.6)	14	(100.0)	4	(28.6)	10	(71.4)
Hypotension	12	1	1	(8.3)	5	(41.7)	1	(8.3)	11	(91.7)
Blister	11	1	1	(9.1)	3	(27.3)	6	(54.5)	5	(45.5)
Tremor	10	1	1	(10.0)	3	(30.0)	1	(10.0)	8	(80.0)
Lymphadenitis	9	4	4	(44.4)	2	(22.2)	1	(11.1)	8	(88.9)
Intussusception	8	7	7	(87.5)	5	(62.5)	8	(100.0)	0	(0.0)
Hypersensitivity	8	1	1	(12.5)	2	(25.0)	1	(12.5)	7	(87.5)

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 to December 2018. Note: for injection site reaction, rash and convulsions, PTs were grouped as described below.

c AEFI records where only one adverse event was reported.

d 'Serious' outcomes are defined in the Methods section.

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

f Percentages relate to the number of AEFI records in which the specific adverse event was listed

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

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

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

n = 10.6%) hexavalent DTPa-IPV-HepB-Hib (n = 426; 10.1%), meningococcal ACWY (n = 396; 9.4%), dTpa (n = 357; n = 8.5%) rotavirus (n = 324; 7.7%), HPV (n = 307; 7.3%), meningococcal B (n = 301; 7.1%), and MMR (n = 301; 7.1%) (Table 4).

Of the 1,261 adverse events following seasonal influenza vaccination, 338 (26.8%) were reported in adults aged  $\geq 65$  years, with most of these following enhanced immunogenicity influenza vaccines, Flud<sup>®</sup> (128) and Fluzone<sup>®</sup> High Dose (195).

There were 396 reported adverse events following meningococcal ACWY vaccination with 53.3% of these (211) in children < 7 years of age (Table 4).

### Adverse events

The most frequently reported adverse events in 2018 were injection site reactions (ISRs) (n = 1,419; 33.6% of total), pyrexia (n = 639; 15.1%), rash (n = 631; 14.9%), vomiting (n = 324; 7.7%), headache (n = 274; 6.5%) and pain (n = 240; 5.7%) (Table 5, Figure 6). Adverse events of particular interest included convulsions (n = 74; 1.8%), hypotonic-hyporesponsive episode (n = 60; 1.4%), anaphylaxis (n = 40; 0.9%), Guillain-Barré Syndrome (GBS) (n = 14; 0.3%) and intussusception (n = 8; 0.2%) (Table 5).

Of the 14 GBS cases, 6 were in adults aged  $\geq 65$  years and 5 of these cases had received an enhanced immunogenicity influenza vaccine.

The number of reports of particular adverse events has changed over time (Figure 6) and these relate to changes in the vaccination schedule (Table 1).

### Serious adverse events

There were variations in the proportions with outcomes defined as serious (Table 4), although these remained generally low as in previous years. The majority of reported adverse events in 2018 were defined as non-serious (n = 3,538,

84%). Sixteen percent of reported adverse events in 2018 were coded as serious, noting that not all reports included detailed or clinically verified data.

Two deaths were reported to the TGA, but no clear causal relationship with vaccination was found.

- A 22-month-old female died in late March 2018, approximately 5 months after receiving a dose of DTPa-containing vaccine and the MMRV vaccine in early November 2017. The child had a >3 month history of a refractory seizure disorder, likely mitochondrial based on genetic testing.
- A 77-year-old male died in late June 2018, a month after receiving an enhanced immunogenicity seasonal trivalent influenza vaccine. He was diagnosed with sporadic Creutzfeldt-Jakob Disease–Heidenhain variant.

Two miscarriages (spontaneous abortion) were reported in this period, noting that spontaneous abortions are known to occur in 11–22% of all pregnancies.<sup>33,34</sup>

- A 27-year-old female who was known to be pregnant was vaccinated with hepatitis B vaccine for occupational purposes, following advice from her physician on the risks and benefits of vaccination. She was previously unvaccinated. She presented to the emergency department 2 days after vaccination with vaginal bleeding and abdominal cramping. Ultrasound showed a pregnancy with an absent yolk sac and she had a miscarriage at the hospital.
- A female patient was vaccinated with a dose of Japanese encephalitis vaccine. Following vaccination, testing confirmed pregnancy. The patient subsequently suffered a miscarriage. The patient had a history of two previous miscarriages. The report did not include information such as the age of the patient, past medical history, medications, date of vaccination, date of miscarriage, or any other

clinical detail but stated that the miscarriage was not thought to be related to the vaccine.

In summary, all deaths following immunisation reported to the TGA were reviewed by the TGA and where relevant, other relevant authorities, based on the information received from reporters. The TGA encourages all reporters to provide sufficient information to allow the TGA to assess any causal relationship between the administration of a vaccine and the adverse event reported. Both deaths were assessed as being most likely due to concomitant disease that was pre-existing at the time of vaccination and both miscarriages were assessed as being unlikely to have been caused by vaccination.

## Discussion

This report uses similar methodology to the previous five annual reports.<sup>2,15,35–37</sup> The use of MedDRA preferred terms for analysis allows for clearer reporting of adverse events, but needs to be taken into account when comparing the data in this report with data from annual reports prior to 2013.

In 2018, there was a 2.9% increase in the AEFI reporting rate compared to the previous year, though reporting rates were not significantly different (with overlapping confidence intervals) in the majority of jurisdictions in 2018 compared with 2017.<sup>37</sup>

This increase was mainly attributable to NIP funding for the meningococcal ACWY conjugate vaccine for all children at 12 months of age; the enhanced trivalent influenza vaccines (high-dose and adjuvanted) for all adults aged  $\geq 65$  years; and also state- and territory-funded annual seasonal influenza vaccination for all children aged 6 months to  $< 5$  years.

There is usually an increase in reporting of adverse events when a new program or scheduled dose is rolled out, as immunisation providers are more likely to report milder, less serious AEFI for vaccines they are not as familiar with, or that are being given to a new population group.

The variation in reporting of injection site reactions is related to changes in the immunisation schedule for vaccines that are known to have higher rates of ISR, including DTPa-containing vaccines, 23vPPV and HPV vaccine.<sup>3–14,38,39</sup> Increases in reported AEFI were largely associated with time periods when new vaccines were added to the NIP, or eligibility extended, including: 7vPCV (2005) and HPV (2007); the extension of seasonal influenza vaccine on the NIP to include persons  $< 65$  years at high risk of influenza in 2010; 13vPCV replacing 7vPCV in July 2011; the extension of HPV to males in 2013; seasonal influenza vaccine funded for Aboriginal and Torres Strait Islander children aged 6 months to  $< 5$  years in 2015; booster dose of DTPa for children at 18 months of age in 2016; zoster vaccine funded for adults aged 70 years with a five year catch-up program for people aged 71–79 years from November 2016; and in 2018, NIP funding for the meningococcal ACWY conjugate vaccine for all children at 12 months of age; the enhanced trivalent influenza vaccines (high-dose and adjuvanted) for all adults aged  $\geq 65$  years; and also state- and territory-funded annual seasonal influenza vaccination for all children aged 6 months to  $< 5$  years.

A reduction and stabilisation of reporting rates over time often occurs thereafter.<sup>2,4,5,7,10,12–15,35–37,40</sup> During this second year of implementation of the zoster vaccination program, there were 135 AEFI reports in adults who received the zoster vaccine, although the majority (83%) were not serious.

Overall, injection site reaction, pyrexia, rash, vomiting, headache and pain were the most commonly reported adverse events to the TGA in 2018. AEFI reporting rates for most individual vaccines in 2018 were similar to those for 2017. These findings are similar to nationally-representative vaccine safety data from AusVaxSafety,<sup>41</sup> which actively monitors the safety of vaccines (e.g. pertussis, zoster, influenza, HPV) in vaccinated people from more than 300 sentinel surveillance sites nationwide. From 1 February 2018, AusVaxSafety monitored the safety of a new HPV vaccine,

Gardasil®9, in 11- to 14-year old adolescents. During the reporting period 1 February 2018 to 31 December 2018, AusVaxSafety received data from 15,959 adolescents aged 11–14 years; 7.9% of those receiving only HPV vaccine, and 9.6% of those receiving HPV and dTpa vaccines, reported an adverse event, demonstrating event rates that were consistent with what are expected according to the existing data. Injection site reactions were the most commonly reported events. Zoster vaccine was monitored by AusVaxSafety through to November 2018. Approximately 17,500 AusVaxSafety participants received zoster vaccine from 1 January 2018; of these participants, approximately 8.0% reported an adverse event, typically an injection site reaction. No safety signals were observed for pertussis, zoster, influenza and HPV vaccines in 2018 in AusVaxSafety.<sup>41</sup>

Overall for data from the AEMS, the majority of AEFI reports detailed non-serious events and no new safety concerns arose during this period (2018). More than half (56.4%) of reported events were in females and 1.5% were reported in Aboriginal and Torres Strait Islander people. Two deaths were reported during 2018, which were assessed as being most likely due to concomitant disease that was pre-existing at the time of vaccination.

## Conclusion

The number of reported AEFI increased slightly in 2018 compared to 2017, though the majority were non-serious transient events. The data reported here are consistent with an overall high level of safety for vaccines used in Australia when administered according to the clinical recommendations contained within the Australian Immunisation Handbook.<sup>16</sup>

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## Appendix

Abbreviations of vaccine types	
BCG	Bacille Calmette-Guérin (i.e. tuberculosis)
DTPa	diphtheria-tetanus-pertussis (acellular) – paediatric formulation
dTpa	diphtheria-tetanus-pertussis (acellular) – adolescent and adult formulation
DTPa-IPV	combined diphtheria-tetanus-pertussis (acellular) and inactivated poliovirus (quadrivalent)
DTPa-IPV-HepB-Hib	combined diphtheria-tetanus-pertussis (acellular), inactivated poliovirus, hepatitis B and <i>Haemophilus influenzae</i> type b vaccine (hexavalent)
HepB	hepatitis B
Hib	<i>Haemophilus influenzae</i> type b
Hib-HepB	combined <i>Haemophilus influenzae</i> type b and hepatitis B
Hib-MenC	combined <i>Haemophilus influenzae</i> type b and meningococcal C conjugate vaccine
HPV	human papillomavirus
MenACWY	quadrivalent meningococcal (serogroups A, C, W-135, Y) conjugate vaccine
MenB	meningococcal B vaccine
MenCCV	meningococcal C conjugate vaccine
MMR	measles-mumps-rubella
MMRV	measles-mumps-rubella-varicella
pH1N1	pandemic H1N1 influenza 2009
7vPCV	7-valent pneumococcal conjugate vaccine
13vPCV	13-valent pneumococcal conjugate vaccine
23vPPV	23-valent pneumococcal polysaccharide vaccine