Public Health Ontario
PARTNERS FOR HEALTH

Santé publique Ontario
PARTENAIRES POUR LA SANTÉ

Annual Report on Vaccine Safety in Ontario, 2015

TECHNICAL REPORT

November 21, 2016

Public Health Ontario

Public Health Ontario is a Crown corporation dedicated to protecting and promoting the health of all Ontarians and reducing inequities in health. Public Health Ontario links public health practitioners, frontline health workers and researchers to the best scientific intelligence and knowledge from around the world.

Public Health Ontario provides expert scientific and technical support to government, local public health units and health care providers relating to the following:

- communicable and infectious diseases
- infection prevention and control
- environmental and occupational health
- emergency preparedness
- health promotion, chronic disease and injury prevention
- public health laboratory services

Public Health Ontario's work also includes surveillance, epidemiology, research, professional development and knowledge services. For more information, visit www.publichealthontario.ca

How to cite this document:

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Annual report on vaccine safety in Ontario, 2015. Toronto, ON: Queen's Printer for Ontario; 2016.

ISSN: 2369-5846

ISBN: 978-1-4606-8706-2

Public Health Ontario acknowledges the financial support of the Ontario Government.

Authors

Tara Harris, RN, MHSc
Nurse Consultant
Immunization and Vaccine-Preventable Diseases, Public Health Ontario

Jyotsna Nair
Health Analyst
Immunization and Vaccine-Preventable Diseases, Public Health Ontario

Kenny Wong, MPH
Epidemiologist
Immunization and Vaccine-Preventable Diseases, Public Health Ontario

Jill Fediurek, RN, MPH
Manager
Immunization and Vaccine-Preventable Diseases, Public Health Ontario

Alexandra Piatkowski
MPH practicum student
Immunization and Vaccine-Preventable Diseases, Public Health Ontario

Shelley L. Deeks, MD, MHSc
Medical Director
Immunization and Vaccine-Preventable Diseases, Public Health Ontario

Acknowledgements

We would like to extend our sincere thanks to immunization providers across the province for their efforts in reporting adverse events following immunization and to public health unit staff for their ongoing commitment to the surveillance of AEFIs which is essential to the assessment of vaccine safety in Ontario.

In addition, we would like to acknowledge Knowledge Services staff at Public Health Ontario including Stacie Carey and Steven Johnson for their support with the production of this document as well as materials to support its public release.

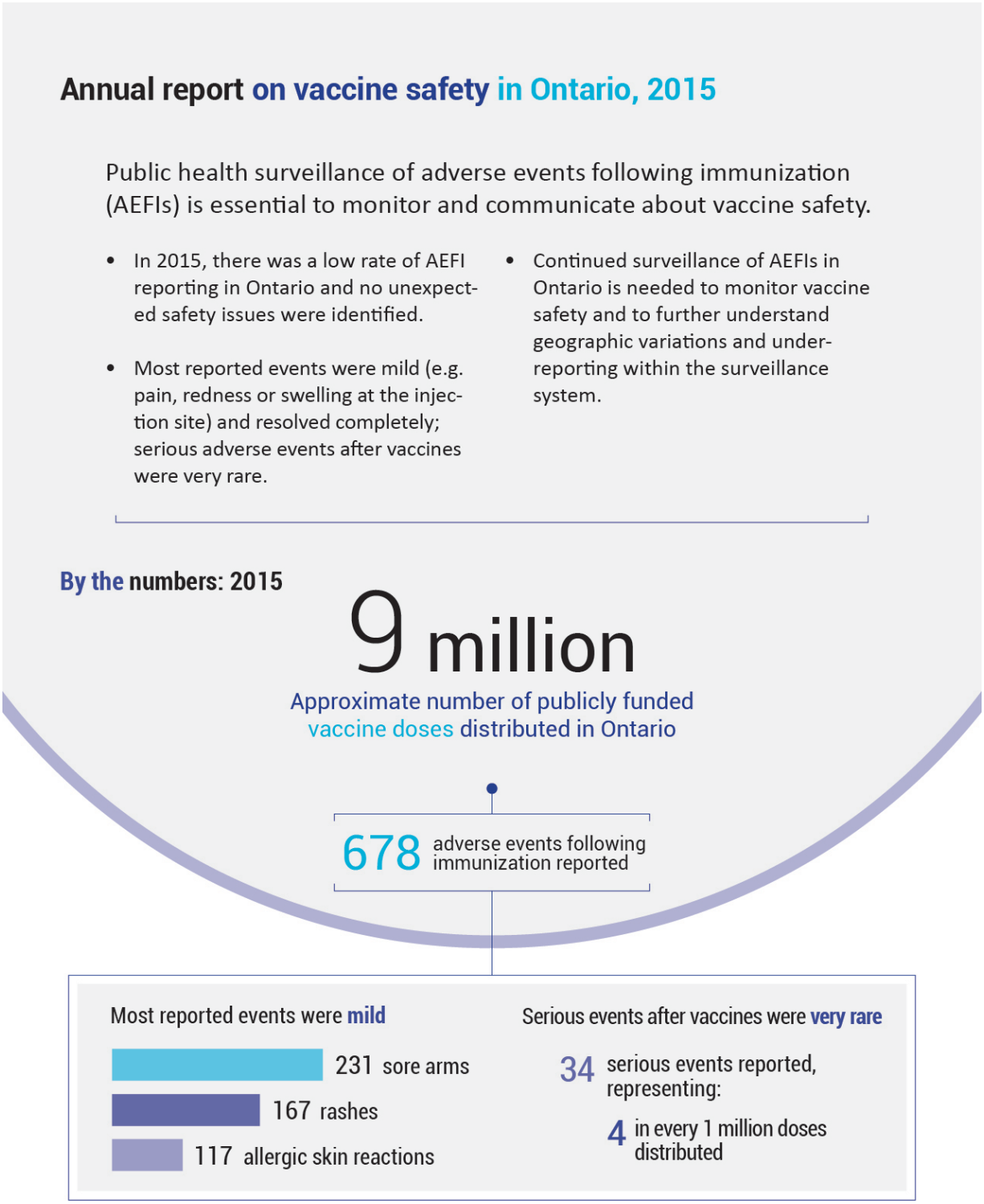
Disclaimer

This document was developed by Public Health Ontario (PHO). PHO provides scientific and technical advice to Ontario's government, public health organizations and healthcare providers. PHOs work is guided by the current best available evidence.

PHO assumes no responsibility for the results of the use of this document by anyone.

Contents

Key messages



Introduction

Public health surveillance of adverse events following immunization (AEFIs) is essential to monitor the safety of vaccines in Ontario. Individual reports of AEFIs provide vital information to help identify previously unrecognized or rare adverse events or an increase in frequency or severity of known adverse events which can be further evaluated. In addition, AEFI surveillance provides valuable information to support publicly funded immunization program planning and communication about the safety of vaccines administered in the province.

AEFI surveillance is a highly collaborative process requiring participation across multiple stakeholders within public health and the broader health care system as well as individual vaccine recipients and their caregivers. In Ontario, public health units (PHUs) play a central role as the primary recipients of AEFI reports, which they investigate and document according to provincial surveillance requirements. PHO coordinates the provincial AEFI surveillance system, working closely with PHUs and the Ministry of Health and Long-Term Care (MOHLTC). For detailed information about roles and responsibilities within Ontario's AEFI surveillance system, as well as the purpose and objectives of conducting AEFI surveillance, please see the Technical Annex of the Annual Report on Vaccine Safety in Ontario.

The Annual Report on Vaccine Safety in Ontario was initiated in 2013 as part of a comprehensive renewal of the provincial vaccine safety surveillance system that included revised provincial case definitions for AEFIs, enhanced surveillance guidelines and forms, improved training and resources for PHUs and information for health care providers. In 2016, PHO undertook an evaluation to assess whether the Annual Report and related products helped public health professionals improve their knowledge and communication about vaccine safety. The findings of this evaluation demonstrated high satisfaction with the report and related resources and recommended specific actions for improvement. This year's report features three key changes based on feedback from PHU stakeholders: (1) reduced length; (2) inclusion of report highlights and key messages; and (3) enhanced data visualization.

Report objectives and scope

The objective of this report is to summarize AEFIs reported in Ontario following vaccines administered in 2015. In addition, reporting trends are assessed by comparison of AEFIs reported in Ontario following vaccines administered across five years between 2011 and 2015.

Methods

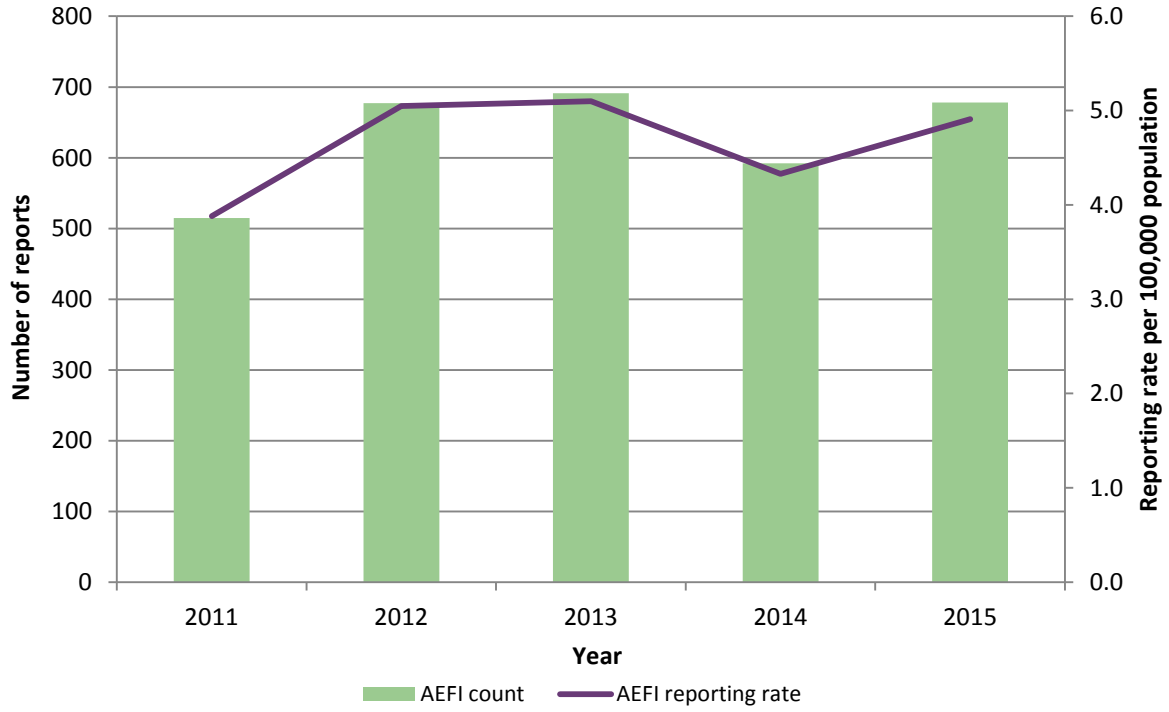
For a detailed description of the provincial AEFI surveillance system and methods for the analysis of AEFI surveillance data, please see the Technical Annex which includes background information on vaccine safety surveillance in Canada, AEFI surveillance reporting processes in Ontario, an in-depth explanation of analytic methods used in the report, and notes on the limitations of AEFI surveillance data.

Trends in reported AEFIs are influenced by changes to the publicly funded immunization program. See the Technical Annex for a description of immunization program changes in recent years.

Results

In Ontario, there were 678 AEFIs reported following vaccines administered in 2015, representing a population-based reporting rate of 4.9 per 100,000 population (Figure 1). The annual reporting rate between 2011 and 2015 ranged from 3.9 to 5.1 per 100,000 population with a significant increasing trend observed over this 5-year period ($p<0.05$).

Figure 1. Number of AEFI reports and reporting rate by year: Ontario, 2011-15



Ontario AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2016/05/01].
Ontario Population: Population Estimates [2015], Statistics Canada, distributed by MOHLTC, received [2014/07/03].

Notes:

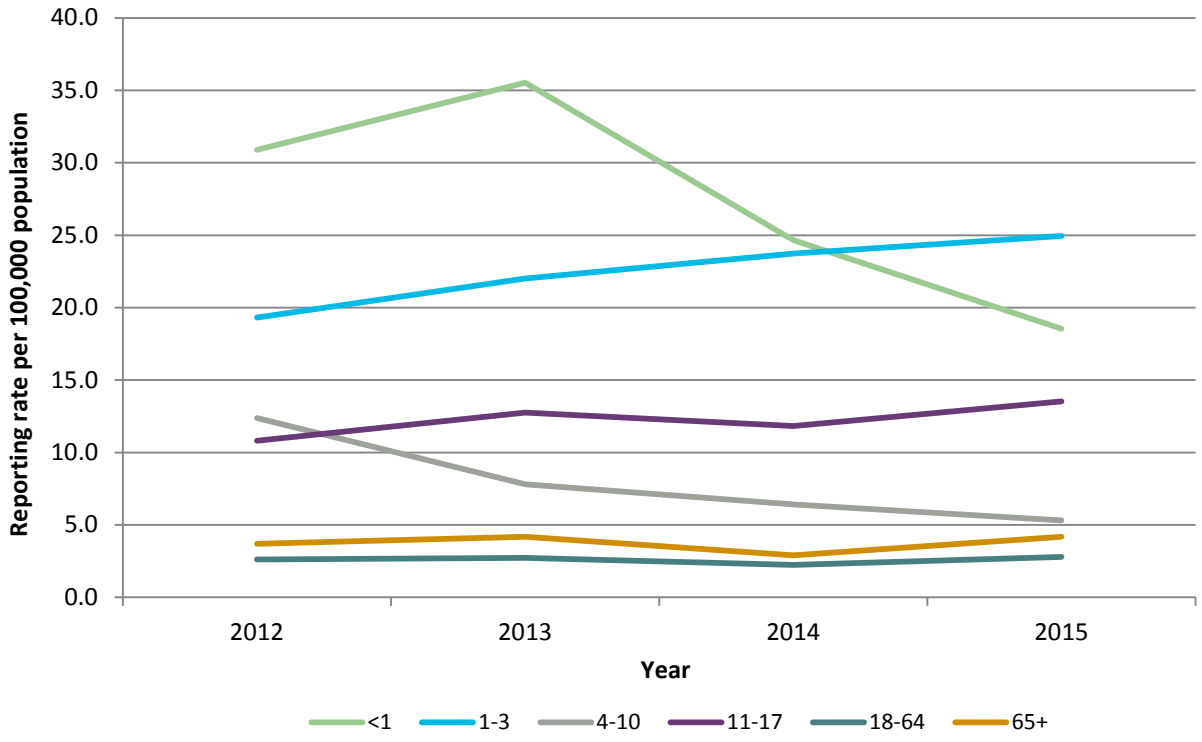
1. Includes only AEFI reports classified as confirmed as per provincial AEFI reporting criteria. See the Technical Annex for more information about provincial AEFI surveillance case classifications.
2. Delayed reports accounted for a 3.8% increase of the total number of confirmed AEFIs in 2011, a 7.3% increase of the total number of confirmed AEFIs in 2012, a 7.6% increase of the total number of confirmed AEFIs in 2013, and a 4.0% increase of the total number of confirmed AEFIs in 2014.

Age and sex distribution

In 2015, persons with AEFI reports ranged in age from one month to ninety-three years (median of 18.5 years) and the proportion of reports were evenly divided between individuals under 18 years and those 18 years of age and older (49.5% vs. 50.5%, respectively).

The highest age-specific AEFI reporting rate was in 1- to 3-year olds (24.9 per 100,000 population) in 2015. Since 2012, the annual age-specific reporting rate for infants under one and children 4- to 10-years old has decreased while there have been increases for 1- to 3 and 11- to 17-year olds over the same time period. The reporting rate for all adults has remained low and stable (Figure 2).

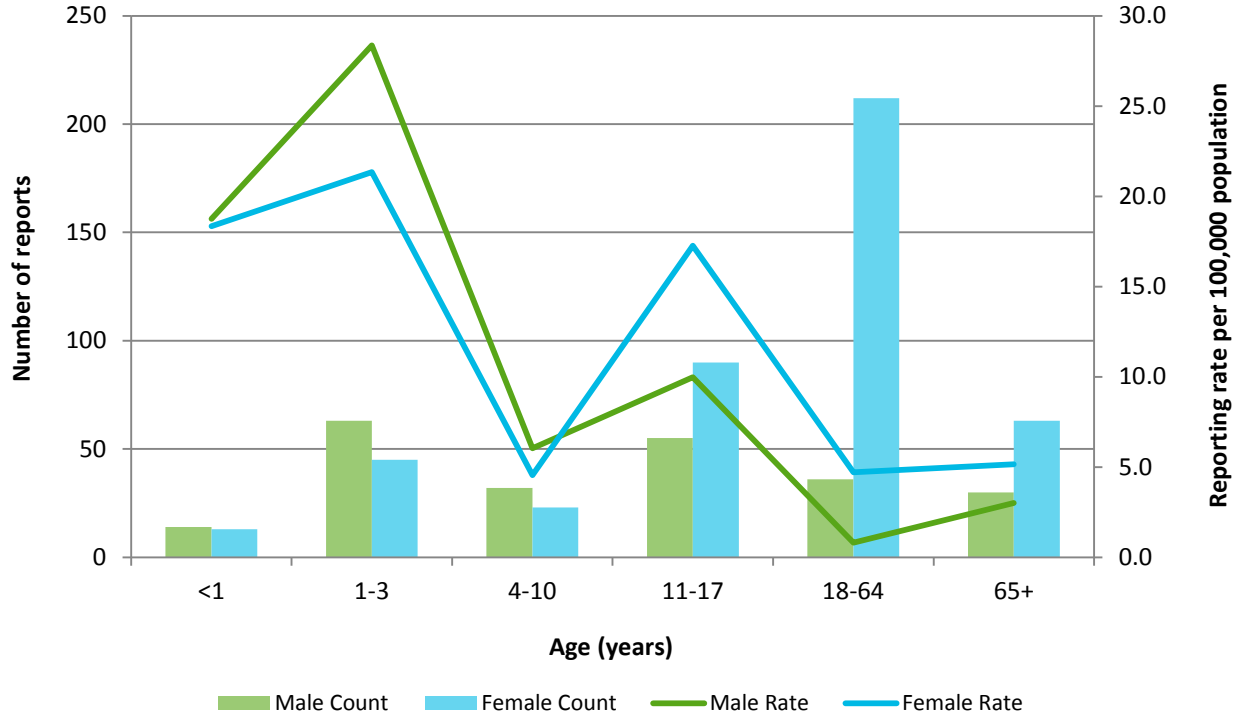
Figure 2. AEFI reporting rate per 100,000 population by age group: Ontario, 2012-15



Ontario AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2016/05/01].
Ontario Population: Population Estimates [2015], Statistics Canada, distributed by MOHLTC, received [2014/07/03].

In 2015, 66.0% of all AEFI reports were female. Female predominance was most pronounced among adults 18- to 64-years of age (female to male reporting rate ratio of 5.8) followed by adolescents 11- to 17-years of age and those 65 years of age and older (both with reporting rate ratios of 1.7) while a male predominance was observed in 1- to 3 and 4- to 10-year old age groups (both with reporting rate ratios of 0.8) (Figure 3). For the 11- to 17-year-olds, the publicly funded HPV vaccination program included females only in 2015, therefore a greater number of reports among females in this age group is expected.

Figure 3. Number of AEFI reports and reporting rates by age group and sex: Ontario, 2015



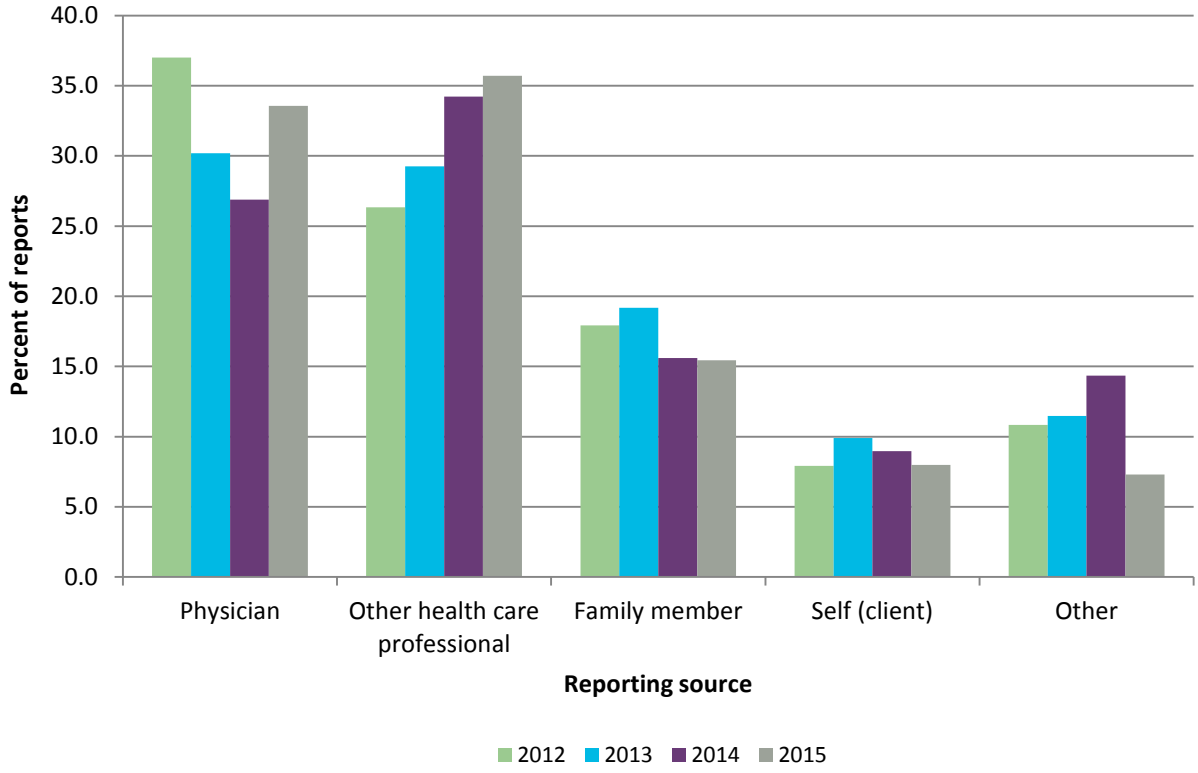
Ontario AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2016/05/01].
Ontario Population: Population Estimates [2015], Statistics Canada, distributed by MOHLTC, received [2014/07/03].
Notes:

1. Two reports are excluded from this figure due to missing information related to age and gender; n=676.

Reporting source

The majority of AEFIs in 2015 were reported by physicians and other healthcare professionals (69.3%; 417/602 reports with reporting source completed). Within this group, the proportion of reports received from physicians increased in 2015 after three years of decline, whereas the proportion of reports from other healthcare professionals (e.g., nurses, pharmacists) has steadily increased since 2012 and exceeded physician reports in 2015 (35.7% vs. 33.6%, respectively) (Figure 4).

Figure 4. Percent distribution of AEFIs by reporting source: Ontario, 2012-15



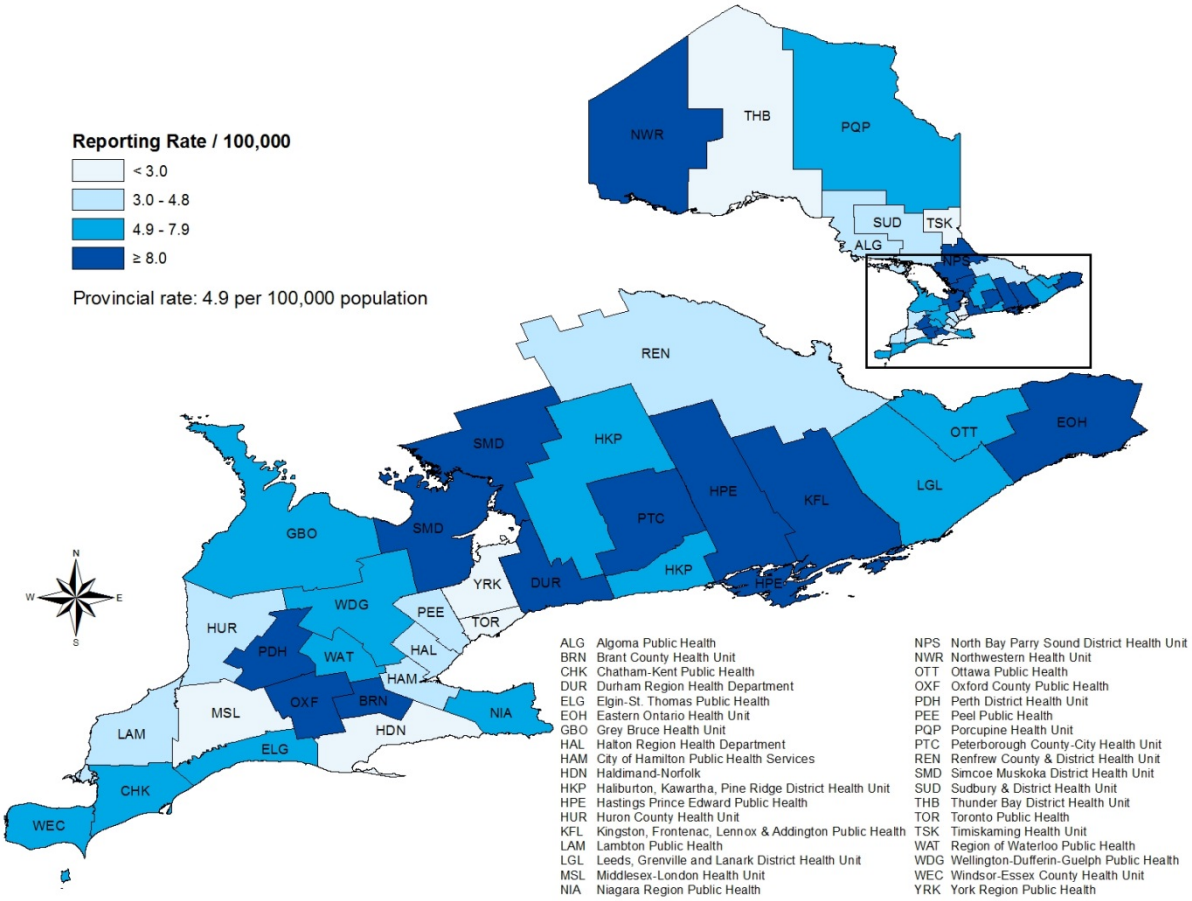
Ontario AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2016/05/01].
Notes:

1. Reporting source 'Other healthcare professional' includes: non-physician healthcare professionals, hospital, health area, or branch office.
2. Reporting source 'Other' includes: Facility, other agency, workplace, personnel, lab, friend, detention centre and other (specify).

Geographic distribution

There was a wide variation in AEFI reporting by PHU in 2015 with PHU-specific reporting rates ranging from 0.4 to 20.5 per 100,000 population. Twenty-two PHUs (61.1%) met or exceeded the overall provincial AEFI reporting rate of 4.9 per 100,000 population, while 14 PHUs were below the provincial reporting rate. This included the three most populated PHUs: Toronto Public Health, Peel Public Health and York Region Public Health (Figure 5). See Appendix 1 for total counts and reporting rates by PHU for 2015.

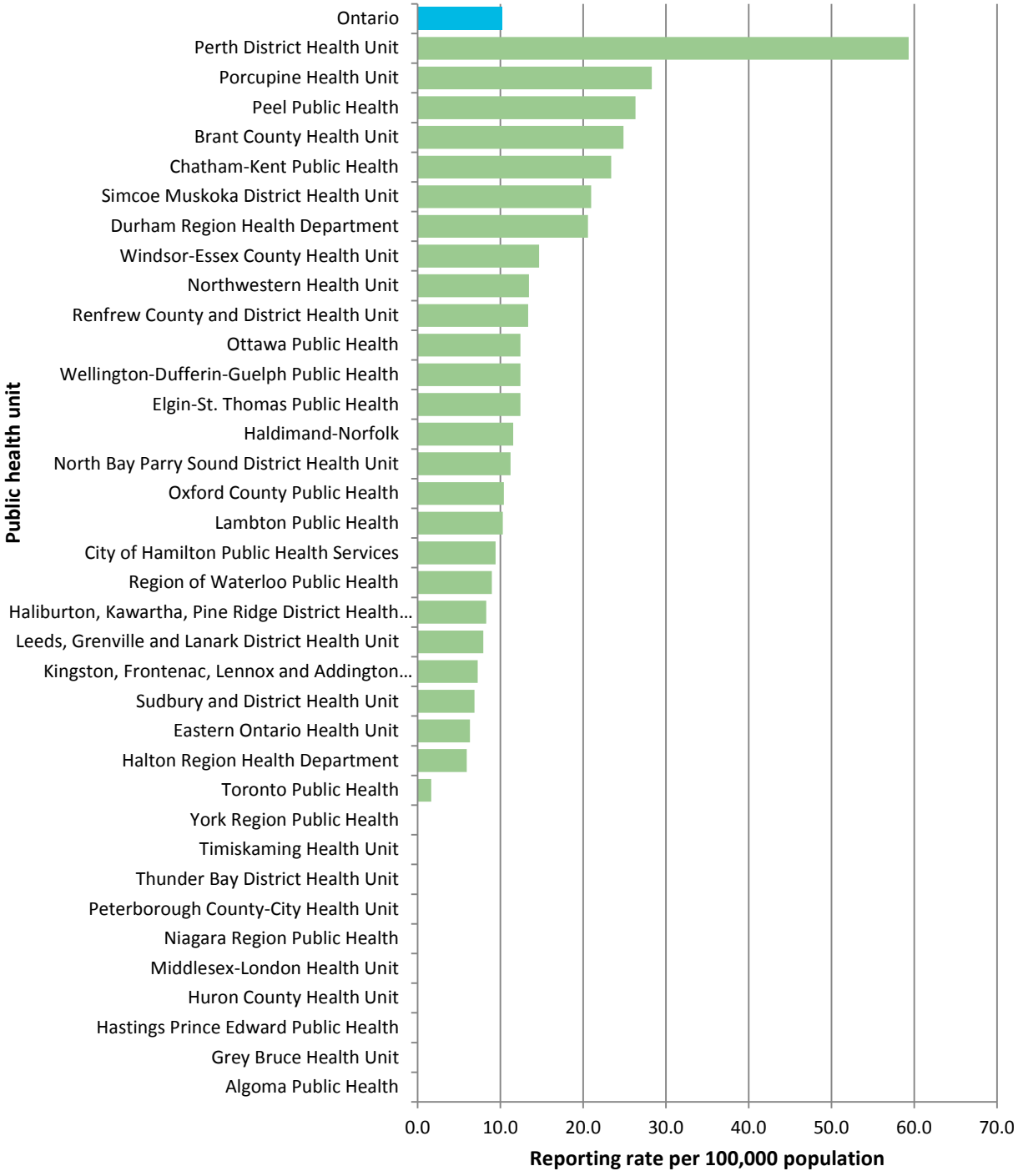
Figure 5. Reporting rates of AEFIs by public health unit: Ontario, 2015



Ontario AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2016/05/01].
Ontario Population: Population Estimates [2015], Statistics Canada, distributed by MOHLTC, received [2014/07/03].

PHU-specific reporting rates also varied widely across the province when looking at AEFIs among 11 -to 17-year olds, for three vaccines that are administered by PHUs in school-based programs (Men-C-ACYW, HB, HPV4) (range: 0.0 to 59.3 per 100,000 population, median 9.2 per 100,000 population). Of note, 10 PHUs had zero AEFI reports in this age group for these three vaccines in 2015 (Figure 6).

Figure 6. Reporting rates for AEFIs among 11- to 17-year olds following Men-C-ACWY, HB, or HPV4 by public health unit: Ontario, 2015



Ontario AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2016/05/01].
Ontario Population: Population Estimates [2015], Statistics Canada, distributed by MOHLTC, received [2014/07/03].

Vaccines

The highest vaccine-specific AEFI reporting rates in 2015 were observed for Men-C-ACWY, HPV4, and Pneu-P-23 (Table 1). Both Men-C-ACWY and HPV4 are delivered through school-based programs and Pneu-P-23 is a vaccine routinely given to persons 65 years and older. All three of these vaccines had low vaccine-specific serious reporting rates. Although influenza vaccine was associated with the highest number of AEFI reports, it had one of the lowest reporting rates.

Trends in reporting rate by vaccine show some variation over time with increases for MMR, Var, Men-C-C and Men-C-ACWY vaccines and decreases for DTaP-IPV, HB and HPV4 vaccines. See Appendix 2 for detailed vaccine-specific rates from 2012 to 2015.

Table 1. Number of AEFI reports and reporting rate by vaccine: Ontario, 2015

Vaccine[1]	Number of AEFI reports by vaccine	Vaccine-specific reporting rate[2]	Number of serious reports	Vaccine-specific serious reporting rate[2]	Doses distributed[3]
Infant and childhood vaccines					
DTaP-IPV-Hib	50	8.7	5	0.9	572,930
Pneu-C-13	58	12.4	7	1.5	466,643
Rot-1	17	6.4	5	1.9	267,441
Men-C-C	39	19.5	3	1.5	200,306
MMR	72	21.0	5	1.5	343,173
Var	56	21.4	4	1.5	262,008
MMRV	16	10.0	3	1.9	160,008
DTaP-IPV	1	18.0	0	0.0	5,557
Tdap-IPV	29	11.9	1	0.4	244,025
Adolescent vaccines					
Men-C-ACWY	57	34.7	1	0.6	164,317
HB	50	19.8	1	0.4	252,370
HPV4	34	23.9	1	0.7	142,191
Tdap	84	10.6	1	0.1	789,275
Routine adult vaccines					
Pneu-P-23	63	23.1	2	0.7	272,289
Td	5	2.0	0	0.0	250,439
Td-IPV	1	5.1	0	0.0	19,501
Universal Influenza Immunization Program (UIIP)					
Inf	157	3.5	12	0.3	4,549,459
Other high-risk publicly funded, travel, and non-publicly funded vaccines					
Chol-Ecol-O	1	-	0	-	-
HA	5	-	0	-	-
HAHB	13	-	0	-	-
HA-Typh-I	1	-	0	-	-

Vaccine[1]	Number of AEFI reports by vaccine	Vaccine-specific reporting rate[2]	Number of serious reports	Vaccine-specific serious reporting rate[2]	Doses distributed[3]
HPV-9	4	-	0	-	-
IPV	1	-	0	-	-
Men-B	3	-	1	-	-
Rab	2	-	1	-	-
Typh-I	2	-	0	-	-
YF	4	-	0	-	-
Zos	58	-	0	-	-

Notes:

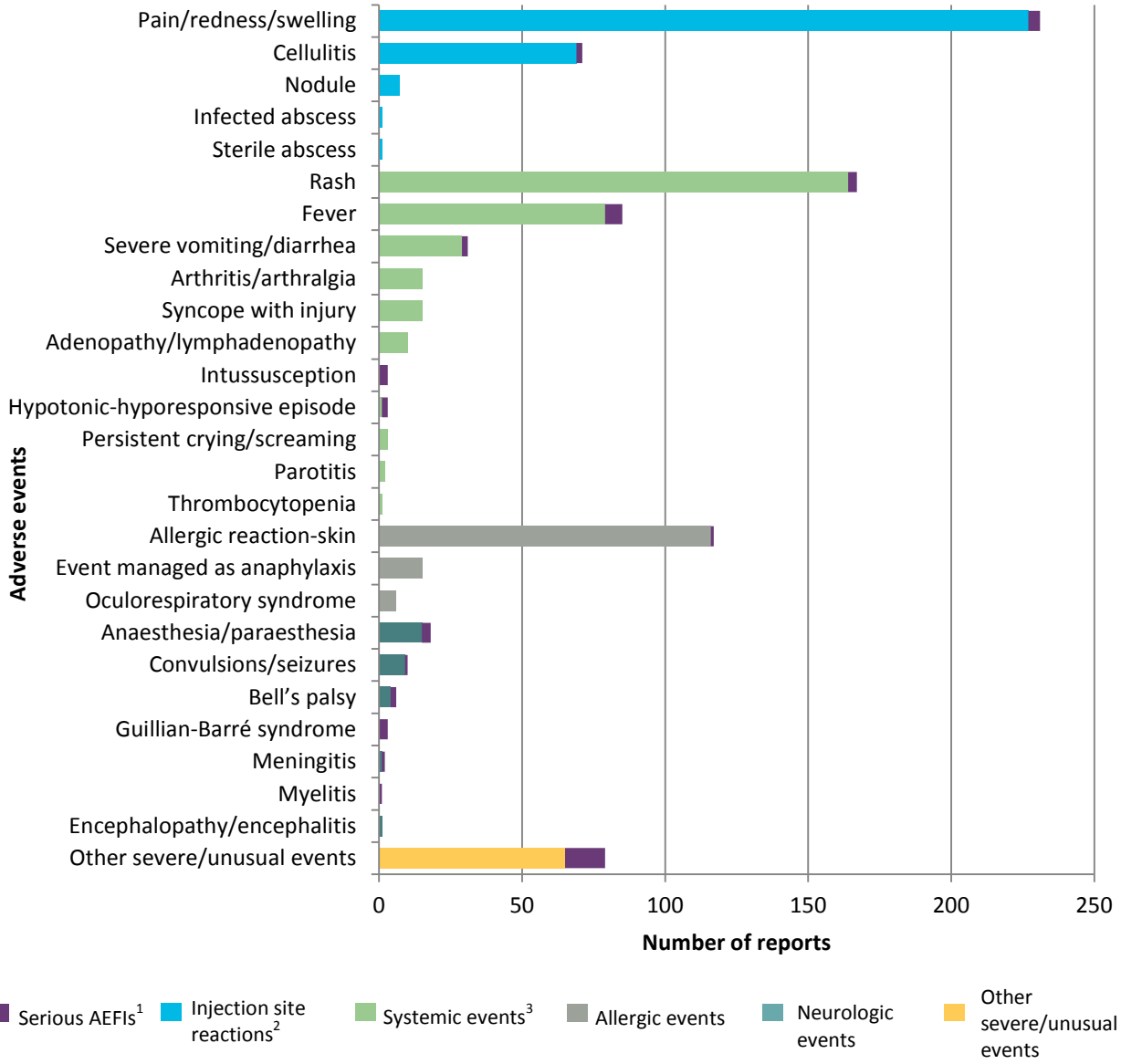
1. Only those vaccines with AEFI reports are shown. See the Technical Annex for a list of all possible vaccines, corresponding vaccine products and agent abbreviations. Vaccines are grouped by recommended age of receipt as per the Publicly Funded Immunization Schedules for Ontario.
2. Vaccine-specific reporting rates per 100,000 doses distributed. Rates are calculated for routine, publicly funded vaccines only.
3. Doses distributed are obtained from Ontario Government Pharmacy and Medical Supply Service (OGPMSS) and reporting rates are calculated for routine publicly funded vaccines only.

In 2015, the combined reporting rate for vaccines (HB, Men-C-ACWY, HPV4 vaccines) primarily delivered by PHUs to adolescents (11- to 17-years-old) in school-based programs was 19.8 per 100,000 doses distributed. The combined reporting rate for vaccines (DTaP-IPV-Hib, Rot-1, Pneu-C-13, MMR, Men-C-C, Var vaccines) primarily administered by primary care providers to children under four years was 5.5 per 100,000 doses distributed. Both the reporting rate for programs primarily delivered by PHUs and the reporting rate for physician-administered agents have increased slightly between 2012 and 2015, but the trend for higher reporting rates among PHU-delivered vaccines continues.

Adverse event descriptions

Adverse events were recorded in 99.6% (n=675) of reports; 95.0% of these were classified as non-serious. The most frequently reported adverse events were pain, redness, or swelling at the injection site, followed by rash and allergic skin reactions (Figure 7).

Figure 7. Number of non-serious and serious AEFI reports by adverse event and category: Ontario, 2015



Ontario AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2016/05/01].

Notes:

1. All serious AEFIs within each event are shaded purple. For serious AEFI definition, please see the Technical Annex.
2. Pain, redness or swelling includes: pain, redness or swelling at the injection site lasting >4 days and/or pain, redness or swelling at the injection site (of any duration) extending beyond the nearest joint.
3. Fever ≥38°C is only reportable in conjunction with another reportable event.

Overall, injection site reactions were recorded in 43.0% of all reports (Table 2) and 97.9% of these were classified as non-serious. Injection site reaction was the only reported adverse event in the majority of these reports (63.4%; n=184). Routinely administered vaccines with the highest reporting rate for injection site reactions were Pneu-P-23, Var and Tdap (19.8, 9.2, 7.1 per 100,000 doses distributed, respectively).

The next most frequently reported adverse event was rash which was present in 24.7% of reports (n=167); 98.2% were not classified as serious. Approximately half of all rash reports (51.5%, n=86) were associated with live virus vaccines (MMR, MMRV, Var, or Zos) and 64.0% (n=55) of live virus vaccine rashes occurred within 5 to 42 days (i.e., the expected time to onset range for live virus vaccines). There were 10 rashes following live virus vaccines that were confirmed as vaccine strain by genotyping, including nine measles vaccine-strain (eight following MMR vaccine, one following MMRV) and one varicella vaccine strain (following varicella vaccine).

Table 2 Number and distribution of AEFI reports by adverse event category: Ontario, 2015

Adverse event category[1]	Adverse event[2]	Number of AEFI reports[3]	Percent of all AEFI reports[4]	Number of serious AEFI reports
Injection site reactions		**290**	**43.0**	**6**
	Cellulitis	71	10.5	2
	Infected abscess	1	0.1	0
	Nodule	7	1.0	0
	Pain/redness/swelling at the injection site[1]	231	34.2	4
	Pain/redness/swelling extending beyond nearest joint	57	8.4	0
	Pain/redness/swelling 4-10 days	150	22.2	1
	Pain/redness/swelling >10 days	47	7.0	3
	Sterile abscess	1	0.1	0
Systemic events		**273**	**40.4**	**13**
	Adenopathy/lymphadenopathy	10	1.5	0
	Arthritis/arthralgia	15	2.2	0
	Fever in conjunction with another reportable event	85	12.6	6
	Hypotonic-hypo-responsive episode (HHE)	3	0.4	2
	Intussusception[5]	3	0.4	3
	Parotitis	2	0.3	0
	Persistent crying/screaming	3	0.4	0
	Rash	167	24.7	3
	Severe vomiting/diarrhea	31	4.6	2
	Syncope with injury	15	2.2	0
	Thrombocytopenia	1	0.1	0
Allergic events		**134**	**19.9**	**1**
	Allergic reaction – skin	117	17.3	1

Adverse event category[1]	Adverse event[2]	Number of AEFI reports[3]	Percent of all AEFI reports[4]	Number of serious AEFI reports
	Event managed as anaphylaxis[5]	15	2.2	0
	Oculorespiratory syndrome (ORS)	6	0.9	0
Neurologic events		**39**	**5.8**	**9**
	Anaesthesia/paraesthesia	18	2.7	3
	Bell's palsy	6	0.9	2
	Convulsions/seizures	10	1.5	1
	Encephalopathy/encephalitis[5]	1	0.1	0
	Guillian-Barré syndrome[5]	3	0.4	3
	Meningitis[5]	2	0.3	1
	Myelitis[5]	1	0.1	1
Other severe/unusual events	Other severe/unusual events	**78**	**11.6**	**14**

Ontario AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2016/05/01].

Notes:

1. Adverse event categories represent groupings of specific types of adverse events and are not mutually exclusive. For category totals, reports with more than one specific event within a category are counted only once. Thus category totals will not sum to the total specific adverse events overall or within a category.
2. Includes only those adverse events where the count was at least one. For a complete list of possible values in iPHIS and corresponding definitions, please see the Technical Annex.
3. Each AEFI report may contain one or more specific adverse events which are not mutually exclusive.
4. Percentages will not sum to 100%. The denominator is the total number of confirmed AEFI reports with at least one adverse event reported (n=675) (three reports had missing adverse events and were therefore excluded).
5. Classified as medically important events.

There were 26 AEFIs reported that were "medically important events," representing 3.8% of all reports. Eight events also met the definition of a serious AEFI and are therefore described under Serious AEFIs, below. Of the remaining 18, there were 15 reports of events managed as anaphylaxis and one report each of thrombocytopenia in a child after influenza vaccine, encephalitis/encephalopathy in a child (subsequently diagnosed as acute ataxia) following varicella vaccine, and meningitis in an adult after HAHB vaccine. Reports of events managed as anaphylaxis ranged in age from 1 to 51 years. The majority (n=9) were following influenza vaccine, three were associated with DTaP-IPV-HIB (including one that also received Var) and one each following Tdap-IPV, HA, and HB given with Men-C-ACWY. The overall reporting rate of anaphylaxis within publicly-funded vaccine programs was 1.6 per million doses distributed. All 15 reports of anaphylaxis were assessed using the Brighton Collaboration standard definition of anaphylaxis. Nine met the Brighton definition with four at level I of diagnostic certainty and five at level II. The remaining reports (n=6) did not have sufficient documented evidence to meet levels I, II or III of diagnostic certainty of the Brighton anaphylaxis case definition.

Serious AEFIs

There were 34 reports of AEFIs that were classified as serious, representing 5.0% (34/678) of all reports. The serious AEFI reporting rate was 2.5 per 1,000,000 population or 3.7 per 1,000,000 doses distributed[1]. The highest vaccine-specific serious reporting rates (using doses distributed as the denominator) were for MMRV and Rot-1 (both 1.9 per 100,000 doses distributed). All serious AEFIs in 2015 were admitted to hospital for a mean length of stay of three days. The majority of serious AEFIs (67.6%; n=23) were under 18 years of age, with most under the age of four years (n=16). There were 11 serious AEFIs that were documented as reported by IMPACT (Immunization Monitoring Program ACTive)[2], ranging from two months to 13 years of age. The proportion of AEFIs defined as serious has remained relatively stable over time with only a slight increase since 2012 (4.4 vs. 5.0% in 2012 and 2015, respectively). Based on case-level review, the most frequent type of adverse event among serious AEFIs in 2015 was febrile illness (29.4%; n=10) including four with rash and two diagnosed as Kawasaki disease. In addition, there were four reports of Guillian-Barré syndrome (GBS), three ataxia in children following live virus vaccines, and three intussusception following rotavirus vaccine. For more information about specific serious AEFI reports, please see Appendix 4.

There were two reports of death in 2015. One was in a child with prolonged hospitalization due to severe, complex medical conditions who was vaccinated during hospital stay. The child developed a varicella vaccine-related rash and subsequently died 27 days after receipt of varicella vaccine. This death was the subject of a coroner's investigation and review by the Pediatric Deaths Under Five Committee of the Office of the Chief Coroner of Ontario, which found the cause of death to be multi-organ system failure due to hypoxia-ischemia of uncertain etiology; perinatal encephalopathy was a contributing factor. The coroner found no link between the event (post-varicella rash) and subsequent death. The second death occurred two days following receipt of influenza and pneumococcal (Pneu-C-13) vaccine in an adult (18-64 years of age) with severe lung disease including sarcoidosis and pulmonary arterial hypertension. The cause of death was reported as cardio-respiratory death.

Healthcare utilization and outcome

Among all AEFI reports in 2015 with healthcare utilization information completed in iPHIS, the majority of individuals sought out-patient medical consultation (74.2%; 493/664). A smaller proportion (21.3%; 144/676) had an emergency room visit and 5.1% (34/670) were admitted to hospital.

In terms of AEFI outcome (completed in 94.3% of reports in 2015), 96.6% were either recovered at the time of assessment (73.9%) or were not yet recovered but likely to recover (22.7%). In a small proportion of reports (3.1%; n=20), the outcome was reported as "residual effects" which refers to

[1] One serious AEFI following a non-publicly funded vaccine was excluded from the reporting rate based on publicly funded doses distributed.

[2] IMPACT is Canada's Immunization Monitoring Program ACTive, is a paediatric hospital-based national active surveillance network for adverse events following immunization, vaccine failures and selected infectious diseases that are, or will be, vaccine preventable. IMPACT has sites in Ontario at the Hospital for Sick Children in Toronto and the Children's Hospital of Eastern Ontario in Ottawa. http://www.cps.ca/en/impact

residual disability or sequelae related to the reported event. In addition, there were two reports of death, which are described in the Serious AEFI section above.

Risk factors

Among all AEFI reports, 22.7% (n=154) had risk factor information completed in iPHIS in 2015. Similar to previous years, for reports with risk factor information completed the most frequent risk factor was "Chronic illness/underlying medical condition" (72.1%; n=111), followed by "Immunocompromised" (5.8%; n=9) and "Immunization program error" (5.2%; n=8). Among immunization program errors, four were related to administration errors (e.g., incorrect land-marking) and four were the result of non-adherence to vaccine indications or recommendations for use (e.g., vaccine contraindicated).

Notes on interpretation

We describe in this report adverse events that were **temporally associated** and not necessarily **causally linked** to vaccines. Our assessment was based on data from iPHIS only and not comprehensive chart review. We provided reporting rate estimates for comparison to other passive surveillance systems and for monitoring reporting trends over time; they should not be interpreted as incidence rates. It is important to note that in the context of a passive AEFI surveillance system, a higher overall reporting rate of AEFIs (across all vaccines) does not necessarily suggest a vaccine safety concern; rather, it is an indicator of a robust passive vaccine safety surveillance system. The quantity of reports contributes to establishing a clear historical baseline that can be used to identify future vaccine safety signals.

Discussion

We assessed AEFIs reported in Ontario following vaccines administered in 2015 and reporting trends since 2011. Overall we found a low rate of AEFI reporting and no unexpected vaccine safety issues. The provincial AEFI reporting rate for vaccines administered in 2015 (4.9 per 100,000 population) was slightly improved compared to 2014. The small but increasing trend observed in the annual reporting rate over the past five years is encouraging; however, Ontario's AEFI reporting continues to be lower relative to other jurisdictions. For example, the most recently published national AEFI reporting rate from 2012 is 10.1 per 100,000 population,[1] more than twice the provincial rate. Under-reporting of AEFIs in Ontario, particularly among healthcare providers, has been highlighted in previous reports.[2-4] Similar to prior years, the 2015 AEFI reporting rates for vaccines delivered mainly by primary care providers were much lower than those delivered mainly by PHUs. Furthermore, reporting rates for vaccines delivered mainly within primary care settings were much lower than expected compared to the national reporting rates for the same vaccines (e.g., MMR: 68.2 vs. 21.0 per 100,000 doses distributed for Canada and Ontario, respectively).[1] AEFI reporting within PHUs may also be an important source of under-reporting as shown by the high variability in AEFI reporting by PHU, particularly for the PHU delivered school-based vaccine programs where there were 10 PHUs in 2015 reporting zero AEFIs for

HB, Men-C-ACWY or HPV4. One recently implemented strategy to address under-reporting includes an AEFI reporting factsheet for healthcare providers, developed by PHO. Starting in July 2016, PHUs were required by the MOHLTC to share this resource during their routine annual cold-chain inspections of all premises in the province that store publicly-funded vaccines. While it is too soon to assess the impact of this initiative, this will be important context for subsequent years when interpreting AEFI reporting trends.

The rate of AEFI reporting within specific age groups in 2015 was consistent with previous years, with higher reporting rates in the youngest age groups. The female predominance in AEFI reports, particularly among adults, is consistently observed within this surveillance system as well as other passive AEFI surveillance systems.[5,6] Additional analysis of this phenomenon in Ontario has shown that female predominance in AEFI reports is seen in vaccines typically administered to adults (Inf, Pneu-P-23, Td) and is less pronounced for serious AEFIs.[7] Further studies are needed to understand the relationship between AEFI reporting and sex.

Reporting of AEFIs by specific vaccine in 2015 was highest for two vaccines primarily delivered by PHUs within school-based programs (HPV4 and Men-C-ACWY), where we tend to have better AEFI reporting, followed by Pneu-P-23, which is known to be a reactogenic vaccine (i.e. injection site reactions), particularly when booster doses are administered at intervals of less than two years.[8] Of note, the rate of reporting of serious events for all of these vaccines was very low.

The types of AEFIs reported in 2015 were similar to previous years in which mild events (e.g. injection site reactions, rash) were the most frequently reported. This is expected based on the safety profile of many vaccines and is consistently observed in AEFI surveillance systems in other jurisdictions.[5,6] It is important to note that while the frequency of these mild events is high relative to other events within the surveillance system, the rate of reporting is very low (e.g., the reporting rate of injection site reactions is 2.1 per 100,000 population). In addition, events such as injection site reactions typically resolve completely on their own and do not pose any contraindication to subsequent doses of vaccine. Similar to 2014, rashes were assessed in more detail in 2015. As expected, approximately half of rash reports were associated with live virus vaccines which are known to produce virus-like rashes, particularly after the first dose (5-10% and 3-5% for MMR and varicella vaccines, respectively).[9,10]

Serious AEFIs were very rarely reported in 2015 and the rate of serious AEFI reporting in Ontario has been stable over time. The types of serious AEFIs reported were most often related to events known to be rarely reported following vaccination. For example, GBS is a rare event which is consistently reported in post-marketing surveillance of vaccines, particularly influenza vaccines. While the evidence of an association between influenza vaccine and GBS is inadequate to accept or reject a causal association,[11] the absolute risk of approximately one excess case of GBS per one million vaccines[12-14] is much lower than that associated with influenza disease.[15,16] Included among serious AEFIs in 2015 were two reports of death which were subject to additional investigation and assessment, and no link to vaccine was made.

For a description of the limitations of the AEFI surveillance system, please see the Technical Annex.

Conclusions

We assessed AEFIs reported in Ontario following vaccines administered in 2015 as well as reporting trends since 2011. Overall, we found a low rate of AEFI reporting and no unexpected vaccine safety issues were identified. The most commonly reported events were mild (e.g. injection site reactions) and serious events were very rare. The majority of individuals were recovered at the time of reporting. Continued surveillance of AEFIs in Ontario is needed to monitor vaccine safety and to further understand geographic variations and under-reporting within the surveillance system.

References

1. Law BJ, Laflèche J, Ahmadipour N, Anyoti H. Canadian Adverse Events Following Immunization Surveillance System (CAEFISS): Annual report for vaccines administered in 2012. CCDR [Internet]. 2014 [cited 2015 Jul 8];40(S-3):7-23. Available from: http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/14vol40/dr-rm40s-3/surveillance-eng.php

2. Annual report on vaccine safety in Ontario, 2012 [Internet]. Toronto, ON: Queen's Printer for Ontario; 2014 Available from: http://www.publichealthontario.ca/en/eRepository/Annual_Report_Vaccine_Safety_Ontario_2012.pdf

3. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Annual report on vaccine safety in Ontario, 2013. Toronto ON: Queen's Printer for Ontario; 2014. Available from: http://www.publichealthontario.ca/en/eRepository/Annual_Report_Vaccine_Safety_Ontario_2013.pdf

4. Annual Report on Vaccine Safety in Ontario, 2014 [Internet]. Toronto, ON: Queen's Printer for Ontario; 2015; cited 2015 Jan 26]. Available from: http://www.publichealthontario.ca/en/BrowseByTopic/InfectiousDiseases/Pages/Vaccine-Safety.aspx#.VK6TPtLF_pU

5. Shimabukuro TT, Nguyen M, Martin D, DeStefano F. Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS). Vaccine. 2015;33(36):4398-405.

6. Mahajan D, Cook J, Dey A, Macartney K, Menzies RI. Annual report: Surveillance of adverse events following immunisation in Australia, 2011. Commun Dis Intell Q Rep. 2012;36(4):E315-32.

7. Harris T, Wong K, Fediurek J, Deeks S. Assessment of Sex-Specific Differences in Adverse Events Following Immunization Reporting in Ontario, Canada. International Conference on Pharmacoepidemiology and Therapeutic Risk Management. Boston, MA.

8. Canadian Immunization Guide. Part 4. Active Vaccines. Pneumoccoccal vaccine. [Internet]. Ottawa ON: Public Health Agency of Canada; 2015 [updated 2015 Mar 24; cited http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-pneu-eng.php].

9. National Advisory Committee on Immunization. Canadian Immunization Guide. Part 4. Active Vaccines. Measles. Ottawa, ON: Public Health Agency of Canada; 2015. Available from: http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-meas-roug-eng.php

10. National Advisory Committee on Immunization. Canadian Immunization Guide. Part 4. Active vaccines. Varicella. [Internet].Ottawa, ON: Public Health Agency of Canada; 2012. Available from: http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-vari-eng.php

11. Institute of Medicine. Adverse effects of vaccines: evidence and causality. Washington, DC: National Academies Press; 2011. [Internet]. Available from: http://www.iom.edu/Reports/2011/Adverse-Effects-of-Vaccines-Evidence-and-Causality.aspx

12. Haber P, DeStefano F., Angulo F, et al. Guillain-Barré syndrome following influenza vaccination. JAMA. 2004(292):2478-81.

13. Juurlink D, Stukel T, Kwong J, et al. Guillain-Barré syndrome after influenza vaccination in adults: a population-based study. Arch Intern Med 2006;166:2217–21.

14. Prothro C, Kudish K, Fielin M. Preliminary results: surveillance for Guillain-Barré syndrome after receipt of influenza A (H1N1) 2009 monovalent vaccine - United States, 2009-2010. MMWR. 2010;59:657-61.

15. Kwong J, Vasa P, Campitelli M, et al. Risk of Guillain-Barré syndrome after seasonal influenza vaccination and influenza health-care encounters: A self-controlled study. The Lancet Infectious Diseases. 2013;13(9):769-76.

16. Hawken S, Kwong JC, Deeks SL, Crowcroft NS, McGeer AJ, Ducharme R, et al. Simulation study of the effect of influenza and influenza vaccination on risk of acquiring Guillain-Barré syndrome. Emerg Infect Dis. 2015;21(2):224-31.

Appendices

Appendix 1: Number of AEFI reports and reporting rate , by public health unit: Ontario, 2015

Public Health Unit	Count	Population	Reporting rate[1]
Ontario	**678**	**13809665**	**4.9**
Perth District Health Unit	16	78191	20.5
Northwestern Health Unit	15	80838	18.6
Eastern Ontario Health Unit	26	206019	12.6
Peterborough County-City Health Unit	17	139989	12.1
North Bay Parry Sound District Health Unit	13	128252	10.1
Brant County Health Unit	13	144698	9.0
Kingston, Frontenac, Lennox & Addington Public Health	18	202545	8.9
Durham Region Health Department	57	661031	8.6
Simcoe Muskoka District Health Unit	44	545712	8.1
Oxford County Public Health	9	112113	8.0
Hastings Prince Edward Public Health	13	163033	8.0
Haliburton, Kawartha, Pine Ridge District Health Unit	14	180948	7.7
Porcupine Health Unit	6	85974	7.0
Chatham-Kent Public Health	7	104743	6.7
Elgin-St. Thomas Public Health	6	91044	6.6
Ottawa Public Health	63	958695	6.6
Leeds, Grenville and Lanark District Health Unit	10	169960	5.9
Grey Bruce Health Unit	9	163639	5.5
Windsor-Essex County Health Unit	22	401588	5.5
Wellington-Dufferin-Guelph Public Health	15	283844	5.3
Region of Waterloo Public Health	28	546595	5.1
Niagara Region Public Health	22	447967	4.9
Halton Region Health Department	26	561319	4.6
Peel Public Health	66	1433973	4.6
Sudbury and District Health Unit	8	199261	4.0
City of Hamilton Public Health Services	22	554453	4.0
Lambton Public Health	5	129689	3.9
Renfrew County and District Health Unit	4	105649	3.8
Algoma Public Health	4	115278	3.5
Huron County Health Unit	2	57822	3.5
Timiskaming Health Unit	1	34304	2.9
Toronto Public Health	80	2839176	2.8
Thunder Bay District Health Unit	3	154998	1.9
York Region Public Health	11	1147492	1.0

Public Health Unit	Count	Population	Reporting rate[1]
Ontario	**678**	**13809665**	**4.9**
Haldimand-Norfolk	1	109408	0.9
Middlesex-London Health Unit	2	469425	0.4

Ontario AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2016/05/01].
Ontario Population: Population Estimates [2015], Statistics Canada, distributed by MOHLTC, received [2014/07/03].
Notes:

1. PHU-specific reporting rates per 100,000 population.

Appendix 2: Number of AEFI reports and reporting rate by vaccine: Ontario, 2012-15

Vaccine[1]	2012		2013		2014		2015	
	Count	Reporting rate[2]	Count	Reporting rate[2]	Count	Reporting rate[2]	Count	Reporting rate[2]
Infant and childhood vaccines								
DTaP-IPV-Hib	62	11.0	72	12.7	55	9.7	50	8.7
Pneu-C-13	48	10.7	55	12.5	54	12.5	58	12.4
Rot-1	23	9.4	25	9.5	21	8.1	17	6.4
Men-C-C	15	9.7	22	14.8	26	16.2	39	19.5
MMR	37	12.8	48	15.9	50	18.4	72	21.0
Var	57	15.4	61	20.1	52	19.7	56	21.4
MMRV	4	14.1	4	14.1	1	1.0	16	10.0
DTaP-IPV	53	103.9	8	340.4	13	N/A	1	18.0
Tdap-IPV	13	9.0	27	13.0	8	3.8	29	11.9
Adolescent vaccines								
Men-C-ACWY	25	21.2	43	36.0	42	25.9	57	34.7
HB	58	24.5	66	24.6	46	17.2	50	19.8
HPV4	47	27.3	48	27.0	38	23.7	34	23.9
Tdap	60	9.0	56	8.3	75	11.9	84	10.6
Routine adult vaccines								
Pneu-P-23	41	20.1	60	25.5	34	14.1	63	23.1
Td	10	3.2	13	4.7	6	2.2	5	2.0
Td-IPV	1	4.1	0	0.0	0	0.0	1	5.1
Universal Influenza Immunization Program (UIIP)								
Inf	199	5.3	187	4.5	151	3.4	157	3.5
Other high-risk publicly funded, travel, and non-publicly funded vaccines								
Chol-Ecol-O	1	-	1	-	1	-	1	-
Men-B	0	-	0	-	3	-	3	-
HA	2	-	3	-	3	-	5	-

Vaccine[1]	2012		2013		2014		2015	
	Count	Reporting rate[2]	Count	Reporting rate[2]	Count	Reporting rate[2]	Count	Reporting rate[2]
HA-Typh-I	3	-	5	-	0	-	1	-
HAHB	10	-	7	-	18	-	13	-
IPV	3	-	0	-	1	-	1	-
Typh-I	6	-	1	-	3	-	2	-
Typh-O	2	-	1	-	1	-	0	-
YF	8	-	7	-	5	-	4	-
Zos	31	-	42	-	40	-	58	-
Rab	4	-	8	-	6	-	2	-
HPV9	0	-	0	-	0	-	4	-
Total AEFIs	677		691		592		678	

Ontario AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2016/05/01].

Notes:

1. Only those vaccines with AEFI reports are shown. See Technical Annexfor a list of all possible vaccines, corresponding vaccine products and agent abbreviations. Vaccines are grouped by recommended age of receipt as per the Publicly Funded Immunization Schedules for Ontario.16 Age of receipt of some vaccines may vary according to immunization status of individuals and vaccine-specific indications.
2. Vaccine-specific reporting rates per 100,000 doses distributed. Doses distributed are obtained from Ontario Government Pharmacy and Medical Supply Service (OGPMSS) for publicly funded vaccines only.

Appendix 3: Number of AEFI reports and reporting rate by adverse event and category, 2012-15

Adverse event/category[1,2]	2012				2013				2014				2015			
	Count[6]	%[7]	Serious count[6]	% Serious[7]	Count[6]	%[7]	Serious count[6]	% Serious[7]	Count[6]	%[7]	Serious count[6]	% Serious[7]	Count[6]	%[7]	Serious count[6]	% Serious[7]
Injection site reactions	**275**	**40.6**	**7**	**2.5**	**281**	**40.7**	**6**	**2.1**	**259**	**43.9**	**7**	**2.7**	**290**	**43.0**	**6**	**2.1**
Cellulitis	61	9.0	6	9.8	63	9.1	5	7.9	47	8.0	5	10.6	71	10.5	2	2.8
Infected abscess	4	0.6	1	25.0	6	0.9	0	0.0	2	0.3	0	0.0	1	0.1	0	0.0
Nodule	23	3.4	0	0.0	11	1.6	0	0.0	14	2.4	0	0.0	7	1.0	0	0.0
Pain/redness/swelling at the injection site[1]	207	30.6	0	0.0	232	33.6	3	1.3	212	35.9	2	0.9	231	34.2	4	1.7
Pain/redness/swelling extending beyond nearest joint	16	2.4	0	0.0	58	8.4	2	3.4	69	11.7	1	1.4	57	8.4	0	0.0
Pain/redness/swelling <4 days[3]	75	11.1	0	0.0	-	-	-	-	-	-	-	-	-	-	-	-
Pain/redness/swelling >4 days[3]	79	11.7	0	0.0	-	-	-	-	-	-	-	-	-	-	-	-
Pain/redness/swelling 4-10 days[4]	60	8.9	0	0.0	155	22.5	1	0.6	128	21.7	2	1.6	150	22.2	1	0.7
Pain/redness/swelling >10 days[4]	21	3.1	0	0.0	39	5.7	0	0.0	36	6.1	0	0	47	7.0	3	6.4
Sterile abscess	7	1.0	0	0.0	0	0.0	0	0.0	4	0.7	0	0	1	0.1	0	0.0
Systemic reactions	**202**	**29.8**	**12**	**5.9**	**258**	**37.4**	**12**	**4.7**	**219**	**37.1**	**9**	**4.1**	**273**	**40.4**	**13**	**4.8**
Adenopathy/ lymphadenopathy	5	0.7	0	0.0	10	1.4	0	0.0	8	1.4	1	12.5	10	1.5	0	0.0
Arthritis/arthralgia	11	1.6	1	9.1	14	2.0	1	7.1	15	2.5	0	0.0	15	2.2	0	0.0
Fever in conjunction with another reportable event	54	8.0	9	16.7	61	8.8	5	8.2	71	12.0	9	12.7	85	12.6	6	7.1
Hypotonic-hypo-responsive episode (HHE)	5	0.7	2	40.0	3	0.4	0	0.0	7	1.2	0	0.0	3	0.4	2	66.7
Intussusception[5]	0	0.0	0	0.0	1	0.1	1	100.0	0	0.0	0	0.0	3	0.4	3	100.0

Adverse event/category[1,2]	2012				2013				2014				2015			
	Count[6]	%[7]	Serious count[6]	% Serious[7]	Count[6]	%[7]	Serious count[6]	% Serious[7]	Count[6]	%[7]	Serious count[6]	% Serious[7]	Count[6]	%[7]	Serious count[6]	% Serious[7]
Parotitis	2	0.3	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	2	0.3	0	0.0
Persistent crying/screaming	6	0.9	1	16.7	6	0.9	0	0.0	7	1.2	1	14.3	3	0.4	0	0.0
Rash	146	21.6	2	1.4	157	22.8	2	1.3	129	21.9	6	4.7	167	24.7	3	1.8
Severe vomiting/diarrhea[4]	6	0.9	1	16.7	35	5.1	4	11.4	25	4.2	2	8.0	31	4.6	2	6.5
Syncope with injury[4]	0	0.0	0	0.0	6	0.9	0	0.0	11	1.9	0	0.0	15	2.2	0	0.0
Thrombocytopenia[5]	0	0.0	0	0.0	2	0.3	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
Allergic events	**175**	**25.8**	**2**	**1.1**	**142**	**20.6**	**1**	**0.7**	**113**	**19.2**	**0**	**0.0**	**134**	**19.9**	**1**	**0.7**
Allergic reaction – other[3]	25	3.7	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Allergic reaction - skin	133	19.6	1	0.8	129	18.7	0	0.0	95	16.1	0	0.0	117	17.3	1	0.9
Event managed as anaphylaxis[5]	20	3.0	1	5.0	17	2.5	1	5.9	12	2.0	0	0.0	15	2.2	0	0.0
Oculorespiratory syndrome (ORS)	6	0.9	0	0.0	1	0.1	0	0.0	6	1.0	0	0.0	6	0.9	0	0.0
Neurologic events	**31**	**4.6**	**11**	**35.5**	**35**	**5.1**	**10**	**28.6**	**24**	**4.1**	**6**	**25**	**39**	**5.8**	**9**	**23.1**
Acute disseminated encephalomyelitis (ADEM)[5]	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Anaesthesia/ paraesthesia[4]	7	1.0	0	0.0	15	2.2	2	13.3	8	1.4	0	0.0	18	2.7	3	16.7
Bell's palsy	3	0.4	0	0.0	2	0.3	0	0.0	2	0.3	0	0.0	6	0.9	2	33.3
Convulsions/seizures	14	2.1	9	64.3	14	2.0	7	50.0	11	1.9	4	36.4	10	1.5	1	10.0
Encephalopathy/ encephalitis[5]	2	0.3	2	100.0	1	0.1	1	100.0	0	0.0	0	0.0	1	0.1	0	0.0
Guillian-Barré Syndrome[5]	2	0.3	1	50.0	1	0.1	1	100.0	1	0.2	0	0.0	3	0.4	3	100.0
Meningitis[5]	0	0.0	0	0.0	1	0.1	0	0.0	2	0.3	2	100.0	2	0.3	1	50.0
Myelitis[5]	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	1	100.0
Paralysis other than Bell's palsy	3	0.4	0	0.0	1	0.1	0	0.0	2	0.3	0	0.0	0	0.0	0	0.0
Other severe/ unusual events	**129**	**19.1**	**9**	**7.0**	**100**	**14.5**	**11**	**11.0**	**85**	**14.4**	**8**	**9.4**	**78**	**11.6**	**14**	**17.9**

Ontario AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2016/05/01].
Notes:

1. Adverse event categories represent groupings of specific types of adverse events and are not mutually exclusive. For category totals, reports with more than one specific event within a category are counted only once. Thus category totals will not be the sum to the total of specific adverse events overall or within a category.
2. Includes only those adverse events where the count was ≥1. For a complete list of possible values in iPHIS and corresponding definitions, please refer to Technical Annex.
3. These adverse event values were discontinued in iPHIS as of January 1, 2013.
4. These adverse event values were added in iPHIS as of January 1, 2013.
5. Medically important events.
6. Data extracted from iPHIS on May 1, 2016. Each AEFI report may contain one or more specific adverse events which are not mutually exclusive.
7. Percentages will not sum to 100%. The denominator is the total number of confirmed AEFI reports with at least one adverse event reported. The total number of confirmed AEFI reports was 675 (three reports had missing adverse events and were therefore excluded), 590 (two reports had missing adverse events and were therefore excluded), 690 (one report had missing adverse events and was therefore excluded), and 677 for 2015, 2014, 2013, and 2012 respectively.

Appendix 4: Summary of serious AEFIs, 2015

Event-type[1]	Number of reports[2]	Age group (years)	Associated vaccines[3]	Additional information
Febrile illness	10	<1 (2 reports) 1-3	Men-B, DTaP-IPV-Hib, MMR, Pneu-C-13, Men-C-C, MMR, Var, Tdap-IPV, MMRV, Inf, Pneu-P-23	4 with rash and 2 diagnosed as Kawasaki Disease
Guillian-Barré syndrome (GBS)	4	11-17 (2 reports) 18-64 (2 reports)	Men-C-ACWY, Tdap, Var, Inf	One reported as Bell's palsy, subsequently diagnosed as atypical GBS
Ataxia	3	1-3	MMR, Var and MMRV	
Intussusception	3	<1	Rot-1	
Hypotonic-hyporesponsive episode (HHE)	2	<1	DTaP-IPV-Hib, Pneu-C-13, Rot-1	
Thrombosis	2	18-64	Inf	
Cellulitis	2	1-3 18-64	Inf, Pneu-P-23	
Meningitis	1	4-10	DTaP-IPV-Hib, MMRV	Also diagnosed with mastoiditis
Acute ischemic stroke	1	1-3	Var	Event occurred within 6 hours of receiving the vaccine.
Transverse myelitis	1	11-17	HB	
Chronic myofascial pain syndrome	1	18-64	Rab	
Pneumonia	1	18-64	Inf	
Anaesthesia/paraesthesia	1	18-64	Inf	Prolonged pain radiating from injection site, tingling in hands and legs

Ontario AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2016/05/01].

Notes:

1. This information is derived from case-level review of all information in iPHIS and not necessarily the selected "adverse event reaction(s)"
2. In addition to reports within this table (n=32), there were two reports of death described above.
3. Includes vaccines that were co-administered.

Public Health Ontario
480 University Avenue, Suite 300
Toronto, Ontario
M5G 1V2

647.260.7100
communications@oahpp.ca
www.publichealthontario.ca