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Annual Report on Vaccine Safety in Ontario, 2017

Surveillance Report

November 2018

Public Health Ontario

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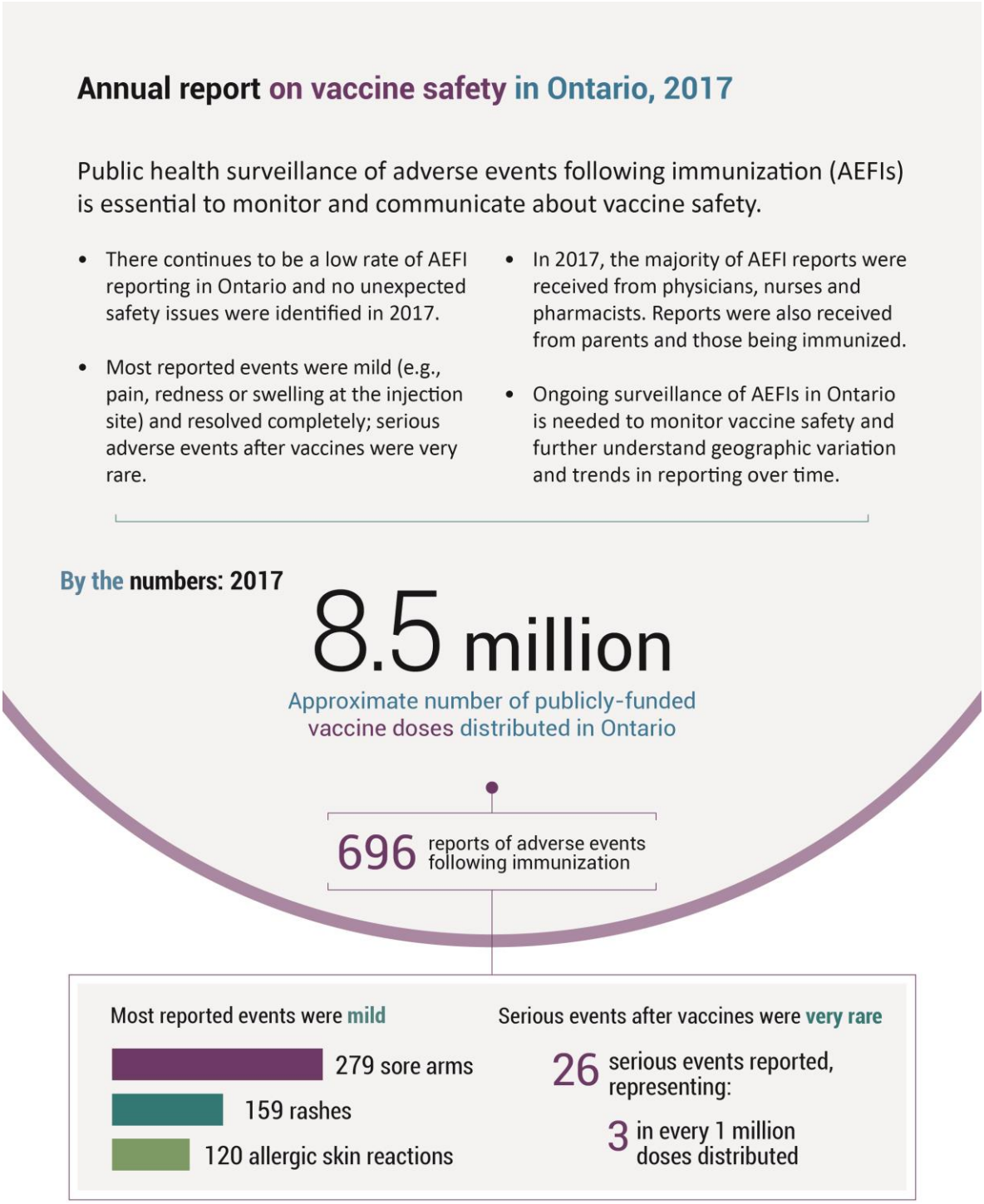
Disclaimer

Contents

Key Messages



Introduction

Public health surveillance of adverse events following immunization (AEFIs) is essential to monitor the safety of vaccines in Ontario. When viewed collectively, 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 then 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. Public Health Ontario (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 (subsequently referred to as the "Technical Annex").

The Annual Report on Vaccine Safety in Ontario was initiated in 2013 as part of a comprehensive renewal of the vaccine safety surveillance system in Ontario. In 2017, PHO launched the Vaccine Safety Surveillance tool, an interactive online tool allowing users to explore, manipulate and download vaccine safety data. Annual vaccine safety data for Ontario are now available through both the Annual Report on Vaccine Safety in Ontario and the interactive online tool.

Report Objectives and Scope

The objective of this report is to summarize AEFIs reported in Ontario following vaccines administered in 2017. In addition, reporting trends are assessed by comparing AEFIs reported in Ontario following vaccines administered across six years between 2012 and 2017.

Methods

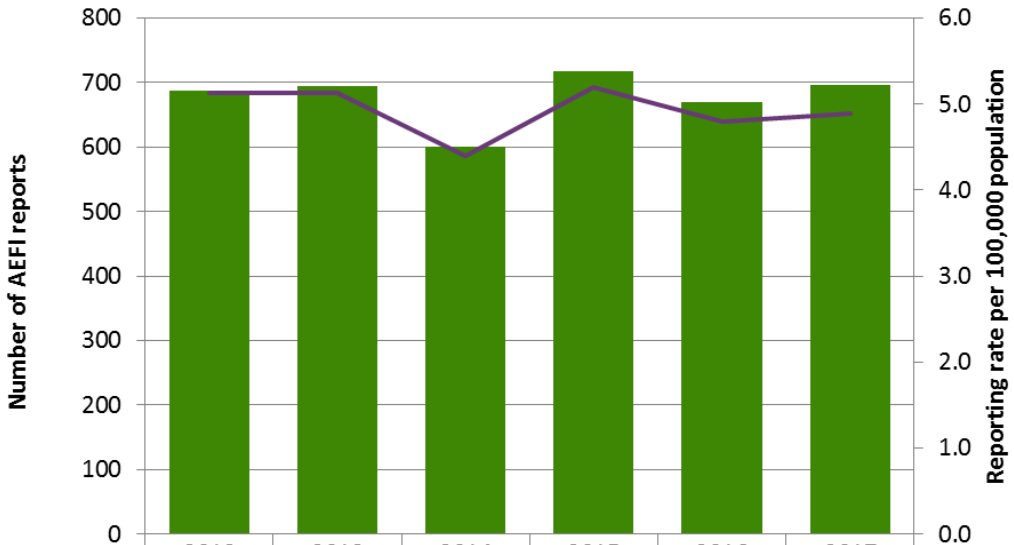
An AEFI report refers to a report received by the PHU, which pertains to one individual vaccine recipient who experiences one or more adverse events that are temporally associated (i.e., the event occurs *after* administration of the vaccine) with receipt of one or more vaccines administered at the same time (i.e., during the same day).

For a detailed description of the provincial AEFI surveillance system, definitions and methods for the analysis of AEFI surveillance data, please see the Technical Annex. The Annex includes details on vaccine safety surveillance in Canada, AEFI surveillance reporting processes in Ontario, an in-depth explanation of analytic methods used in this safety report and notes on the limitations of AEFI surveillance data. Trends in reported AEFIs are influenced by many factors including changes to the publicly-funded immunization program. The 2017 report also includes delayed reports received since the data were extracted for the 2016 Annual Report on Vaccine Safety in Ontario. As some delayed reports may relate to immunizations administered in previous years, annual numbers may differ slightly from past reports. For a complete list of vaccine acronyms used in this report and a description of immunization program changes in recent years, see Appendix 1 and Appendix 3, respectively, of the Technical Annex.

Results

In Ontario, 696 AEFI reports were received following vaccines administered in 2017, representing a population-based reporting rate of 4.9 per 100,000 population (Figure 1). The annual reporting rate between 2012 and 2017 ranged from 4.4 to 5.2 per 100,000 population with no statistically significant change in trends observed over this six-year period. The addition of delayed reports (i.e., reports received in 2017 from vaccines administered in previous years) accounted for <1% increase of the total number of confirmed AEFI reports in 2012 to 2015 and 6.3% increase in 2016, compared to the numbers reported in the 2016 report.

Figure 1. Number of Reports and Reporting Rate of AEFIs per 100,000 Population by Year: Ontario, 2012-17



	2012	2013	2014	2015	2016	2017
Number of AEFI reports	688	695	601	717	670	696
AEFI Reporting rate	5.1	5.1	4.4	5.2	4.8	4.9

AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

Population: IntelliHEALTH Ontario[1,2]

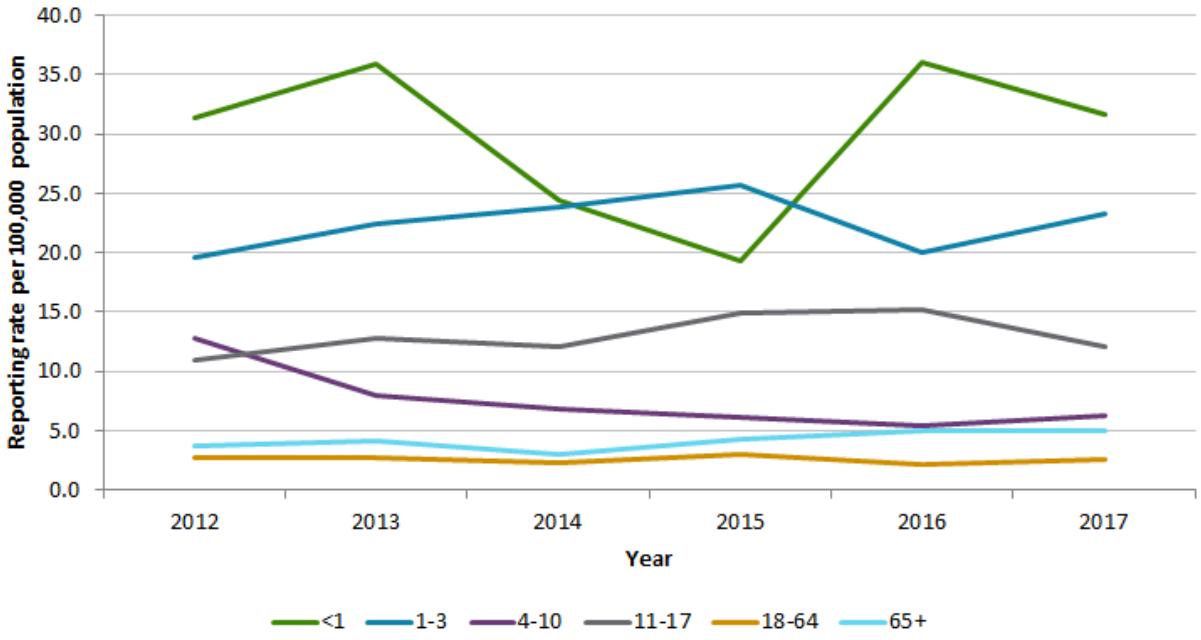
Note: Only includes AEFI reports classified as confirmed, as per provincial AEFI reporting criteria. See the Technical Annex for more information about provincial AEFI surveillance case classifications.

Age and Sex Distribution

In 2017, persons with AEFI reports ranged in age from one month to 91 years, with a median age of 18 years. Similar to previous years, approximately half of all reports were among those younger than 18 years of age (49.6% of total AEFI reports).

Among specific age categories, the highest AEFI reporting rate in 2017 was in infants under one year (31.6 per 100,000 population), followed by children aged one to three years (23.3 per 100,000 population) (Figure 2). The annual age-specific reporting rate for infants under one year declined in 2017, following an increase in 2016, while the annual reporting rate for one- to three-year-olds increased in 2017 after a decline in 2016. Among 11- to 17-year olds, the rate declined in 2017 after increasing between 2012 and 2016. Among four- to 10-year-olds, the rate in 2017 increased after a decline between 2012 and 2016. The reporting rate for adults 18 to 64 years old has remained low and relatively stable. Following an increase between 2014 and 2016, the AEFI reporting rate in the 65 years and older age group remained the same in 2017 compared to 2016, despite 2017 being the first full year of a publicly-funded immunization program for zoster among adults 65 to 70 year olds; this program was introduced in September 1, 2016.

Figure 2. Annual AEFI Reporting Rate per 100,000 Population by Age Group: Ontario, 2012-17



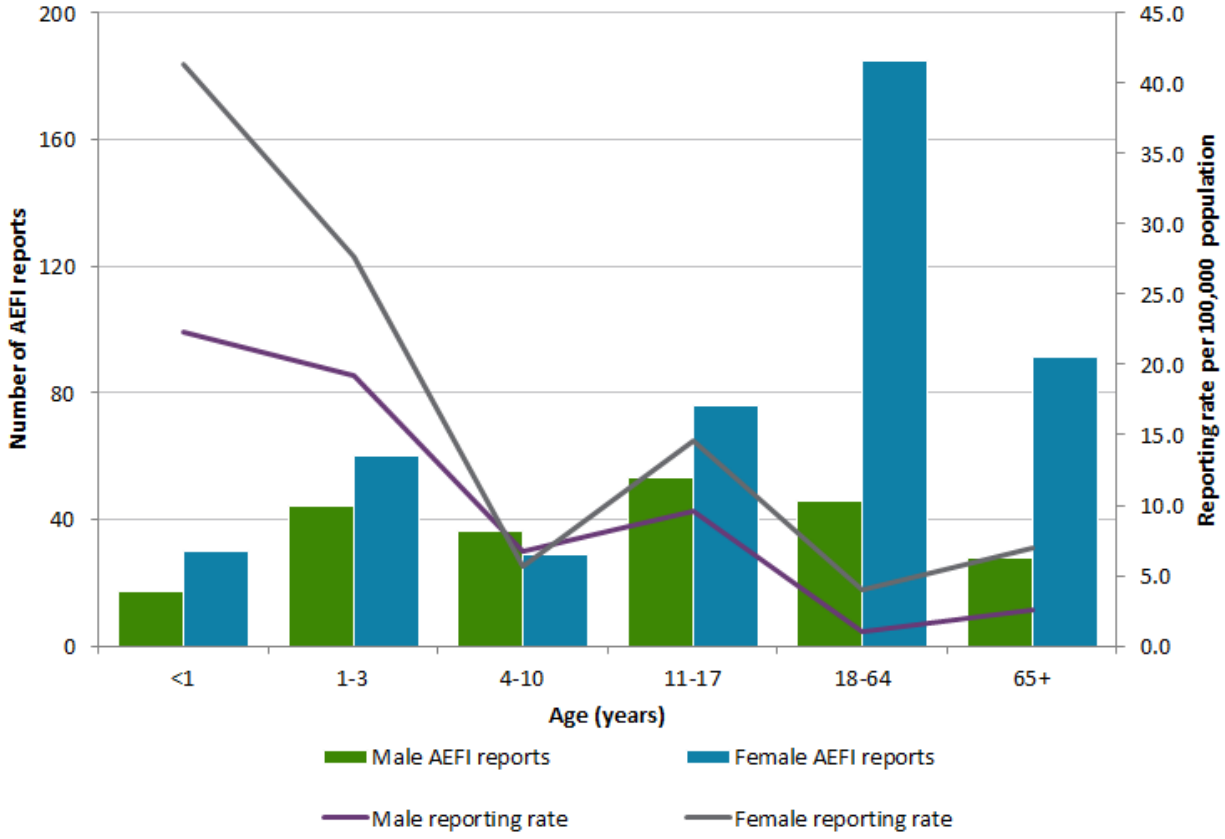
AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

Population: IntelliHEALTH Ontario[1,2]

Note: Excludes five reports with unknown age.

In 2017, the majority of all AEFI reports were in females (67.8%). Male predominance was observed only in the four to 10-year age group, where the female-to-male reporting rate ratio (RRR) was 0.8 (Figure 3). In all other age groups, female predominance was observed, which was most pronounced among adults aged 18 to 64 years (RRR=4.0) followed by adults aged 65 years and older (RRR=2.7). There was a slight reduction in the RRR among 11 to 17 year olds in 2017 compared to 2016 (1.7 in 2016 and 1.5 in 2017). Of note, the publicly-funded HPV vaccination program was expanded to include boys in September 2016.

Figure 3. Number of Reports and Reporting Rates of AEFIs per 100,000 Population by Age Group and Sex: Ontario, 2017



AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

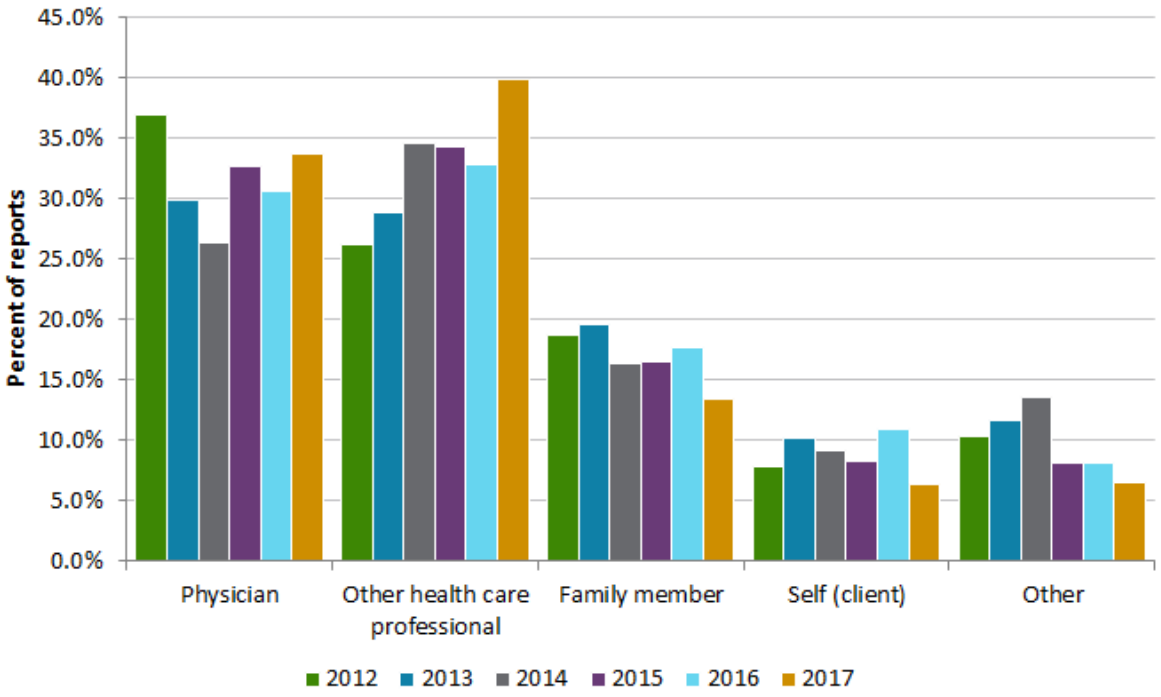
Population: IntelliHEALTH Ontario[2]

Note: Excludes one report with unknown age.

Reporting Source

In 2017, the majority of AEFIs were reported by physicians and other healthcare professionals (73.5%; 458 of 623 reports with reporting source completed) – consistent with what was observed in previous years (Figure 4). The proportion of reports received from physicians has fluctuated over the six-year period, whereas the proportion of reports from other healthcare professionals (e.g., nurses, pharmacists) has generally increased since 2012 and exceeded physician reports since 2014. In particular, the proportion of reports from other healthcare professionals increased from 26% in 2012 to 40% of all reports in 2017, representing the largest increase among all categories. Of note, pharmacists started administering influenza vaccines (to adults and children five years of age and older) as part of the universal influenza immunization program (UIIP) in Ontario in 2012.

Figure 4. Percent Distribution of AEFIs by Reporting Source: Ontario, 2012-17



AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

Notes:

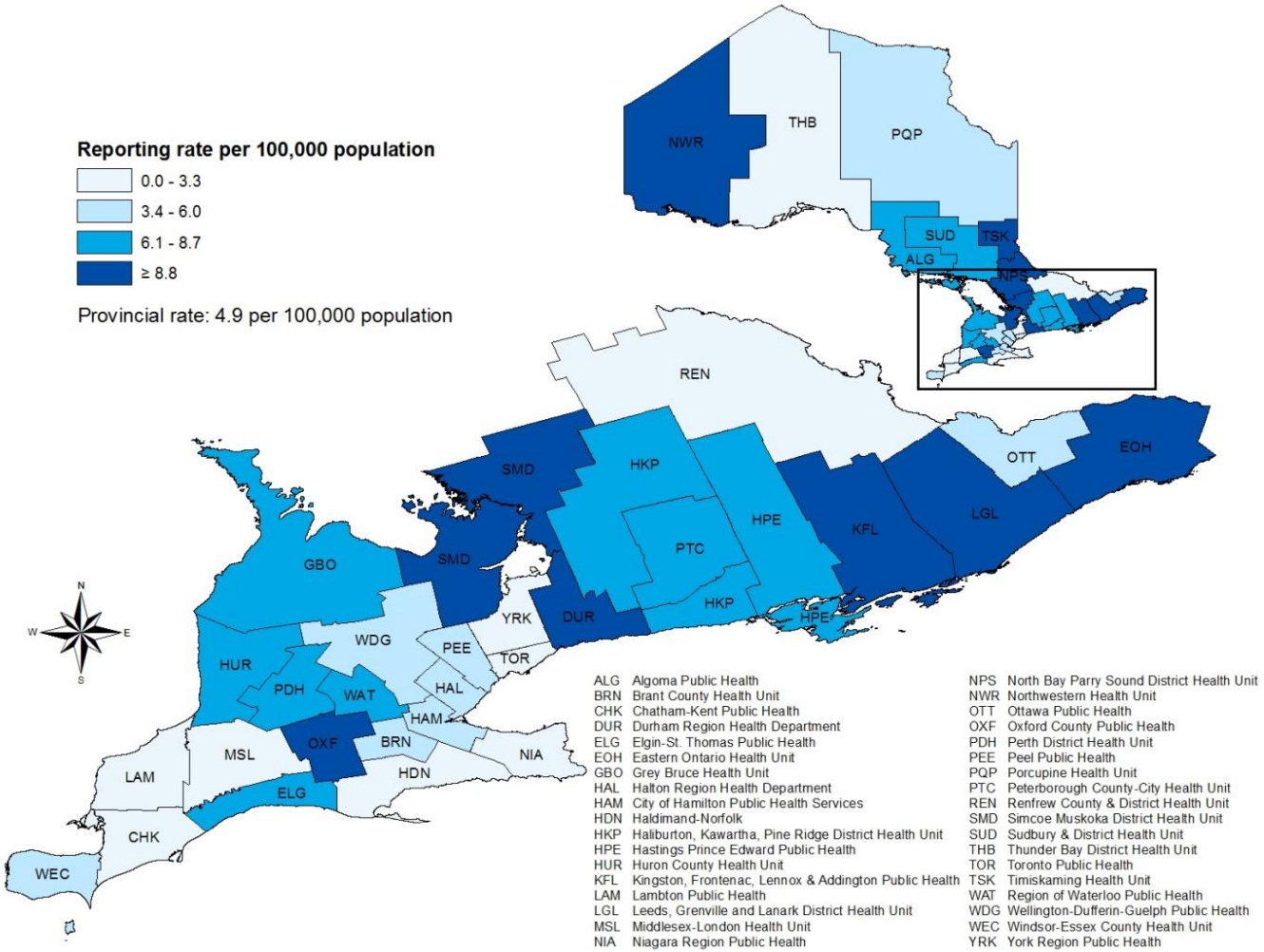
- Excludes 382 reports between 2012 and 2017 with unknown reporting source.
- Reporting source 'Other healthcare professional' includes the following iPHIS values: healthcare professionals, hospital, health area, lab and branch office.
- Reporting source 'Other' includes the following iPHIS values: Facility, insurance, other agency, workplace, personnel, friend, detention centre and other (specify).

Geographic Distribution

All Vaccines

There was a wide variation in AEFI reporting by PHU in 2017 with PHU-specific reporting rates ranging from 0.0 to 22.0 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 in 2017, while the remainder (14 PHUs) were below the provincial rate, including the three most populated PHUs (Figure 5). This represents a slightly higher proportion of PHUs exceeding the provincial rate compared to 2016 (55.6%, 20/36 PHUs). One PHU did not report any AEFIs in 2017. There were two PHUs that did not report AEFIs in any of the three categories discussed in detail below (i.e., following routine infant and early childhood vaccines, school-based vaccines and following influenza vaccine), which was lower compared to 2016 where six PHUs did not report AEFIs in any of these categories. See Appendix 1 for the total number of reports and reporting rates by PHU in 2017. Geographic variation was also observed when reporting rates were grouped by the three vaccine categories and age groups, as shown in the following sections.

Figure 5. AEFI Reporting Rate per 100,000 Population by Public Health Unit: Ontario, 2017



AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

Population: IntelliHEALTH Ontario[2]

Routine Infant and Early Childhood Vaccine Series

The rate of AEFI reporting for infants and young children (i.e., under four years of age) for the six vaccines that are typically delivered by a primary health care provider as part of the routine infant and early childhood vaccine series (DTaP-IPV-Hib, Rot-1, Pneu-C-13, MMR, Men-C-C, and Var) was determined for each PHU. The PHU-specific reporting rates ranged from zero to 109.0 per 100,000 population and the overall provincial rate was 22.4 per 100,000 population. There were seven PHUs that reported zero AEFIs among this age group for any of these six vaccines (Figure 6), compared to 10 PHUs in 2016.

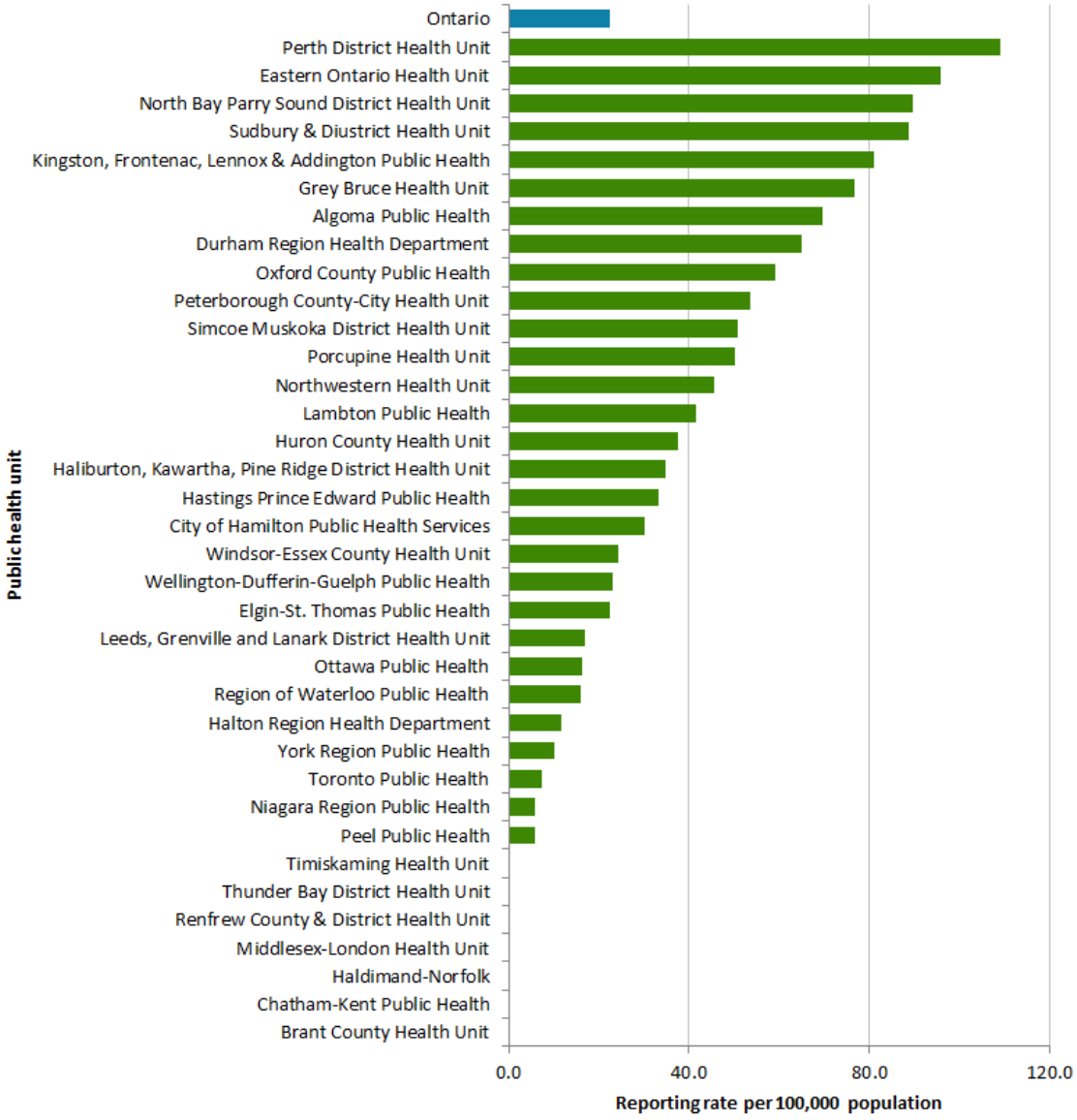
School-Based Vaccines

Among 11- to 17-year-olds, the PHU-specific reporting rate for AEFIs following the four vaccines that are administered to adolescents by PHUs in school-based programs (Men-C-ACYW, HB, HPV4 and HPV9) ranged from zero to 43.6 per 100,000 population, with a provincial rate of 9.7 per 100,000 population. Twelve PHUs did not report any AEFIs for these three vaccines in this age group in 2017 (Figure 7), compared to 15 PHUs in 2016. Of note, HPV9 replaced HPV4 in the Grade 7 school-based program for boys and girls in September 2017 (refer to Technical Annex for further description on program changes).

Influenza Vaccine

In 2017, 4,037,049 net doses of influenza vaccine were distributed throughout the province (refer to Technical Annex on derivation of doses distributed). Rates of influenza AEFI reports are calculated per 100,000 doses distributed, both by doses distributed within each PHU and provincially (reporting rates per 100,000 population are available in the online Vaccine Safety Surveillance tool). The overall PHU-specific reporting rates following influenza vaccine ranged from zero to 30.3 per 100,000 doses distributed, with a provincial rate of 4.1 per 100,000 doses distributed. Six PHUs did not report any AEFIs following administration of influenza vaccine in 2017 (Figure 8), compared to 10 PHUs in 2016.

Figure 6. Reporting Rate per 100,000 Population for AEFIs Among Infants and Children Under Four Years of Age Following DTaP-IPV-Hib, Rot-1, Pneu-C-13, MMR, Men-C-C, or Var Vaccines by Public Health Unit: Ontario, 2017

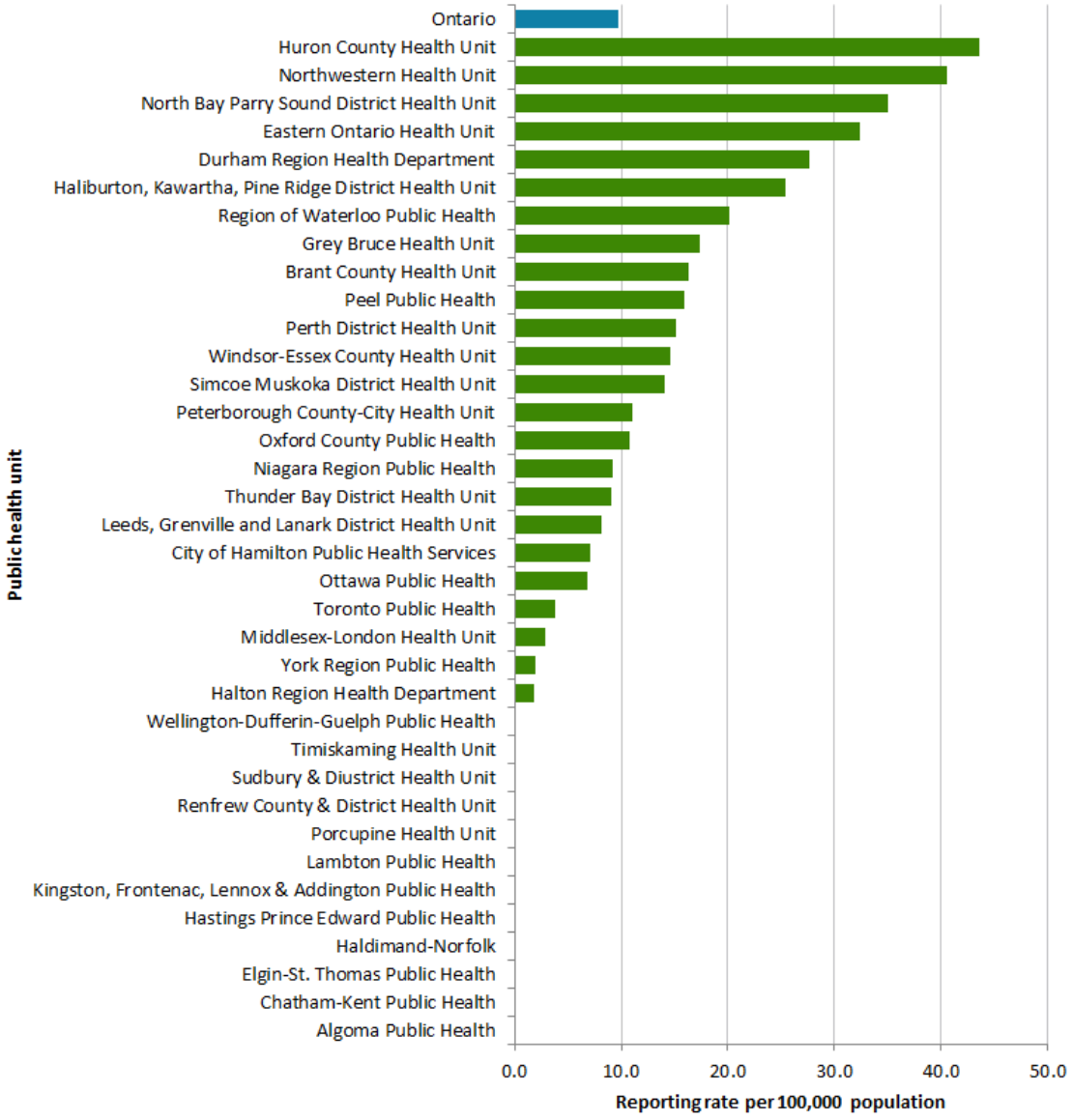


AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

Population: IntelliHEALTH Ontario[2]

Note: Reporting rate includes AEFIs reported among children under four years of age following administration of at least one of the following six vaccines: DTaP-IPV-Hib, Rot-1, Pneu-C-13, MMR, Men-C-C, or Var. Individuals may have received more than one of the specified vaccines at the same time; however, individuals are only counted once in the calculation of the reporting rate.

Figure 7. Reporting Rate per 100,000 Population for AEFIs Among 11- to 17-Year-Olds Following Men-C-ACWY, HB, HPV4 or HPV9 Vaccine by Public Health Unit: Ontario, 2017

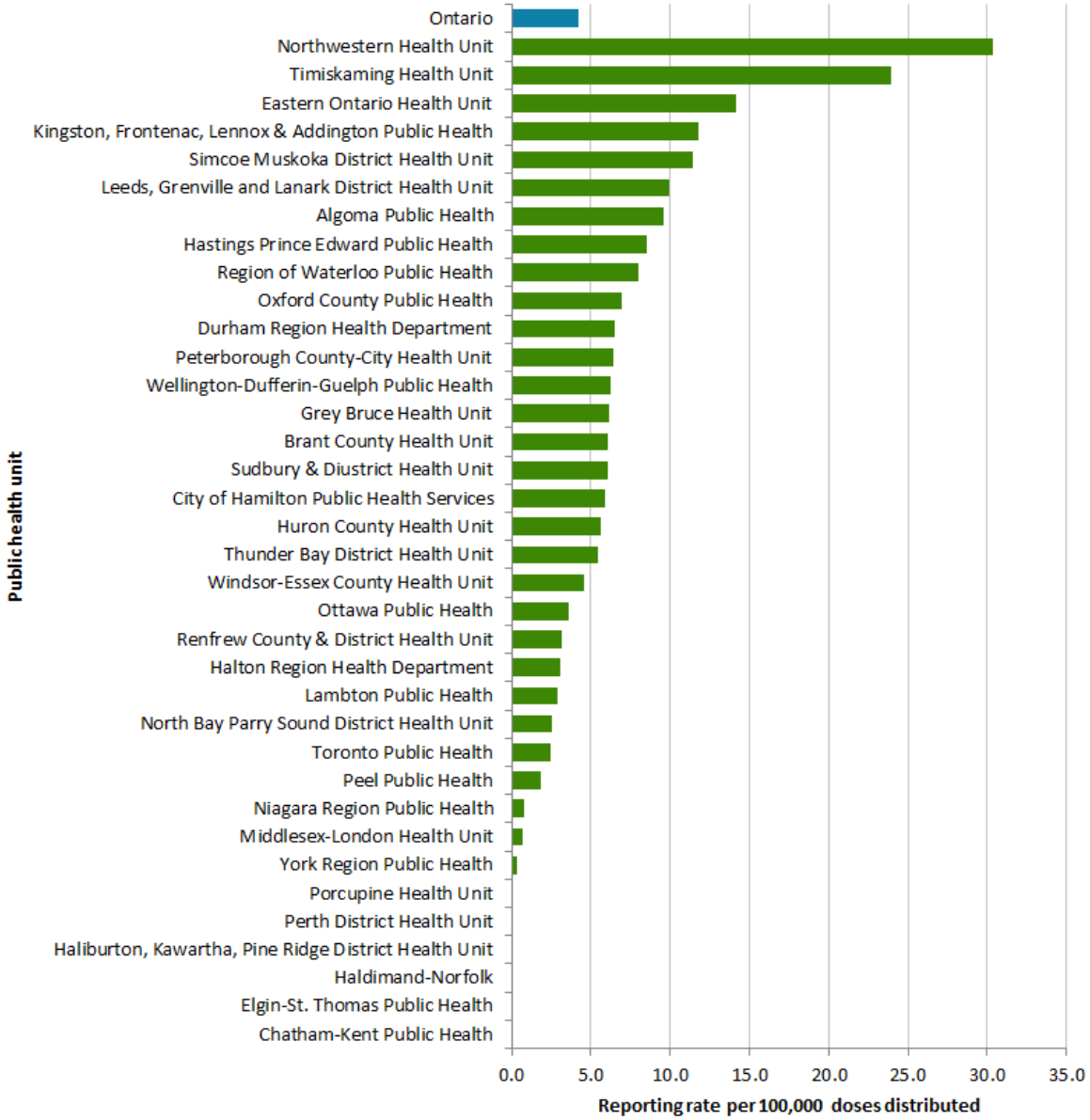


AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

Population: IntelliHEALTH Ontario[2]

Note: Reporting rate includes AEFIs reported among adolescents aged 11 to 17 years, following administration of at least one of the following four vaccines: Men-C-ACYW, HB, HPV4 or HPV9. In September 2017, HPV9 replaced HPV4 in the school-based program. Individuals may have received more than one of the specified vaccines; however, individuals are only counted once in the calculation of the reporting rate.

Figure 8. Reporting Rate per 100,000 Doses Distributed for AEFIs Following Influenza Vaccine by Public Health Unit: Ontario, 2017



AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

Vaccine doses distributed: MOHLTC, Panorama Enhanced Analytical Reporting, extracted by MOHLTC [2018/05/08]

Vaccines

In 2017, there were approximately 8.5 million doses of vaccines distributed in Ontario for the publicly-funded immunization programs. Using net doses distributed for each routine, publicly-funded vaccine as the denominator, the highest vaccine-specific AEFI reporting rates in 2017 were observed for Zos, HPV9 and Men-C-ACWY vaccines (40.4, 35.0, 32.8 per 100,000 doses distributed, respectively; Table 1). Both HPV9 and Men-C-ACWY vaccines are delivered through school-based programs and Zos became a publicly-funded vaccine program for persons between 65 and 70 years old in September 2016; thus, 2017 represents the first year a doses distributed rate could be determined for Zos. A summary of recent changes to the publicly-funded immunization programs is provided in the Technical Annex. Although influenza vaccine was associated with the highest number of AEFI reports, it had the second lowest AEFI reporting rate due to the high volume of doses distributed.

Overall, vaccine-specific serious AEFI reporting rates for all vaccines for which rates could be derived ranged between zero and 3.1 per 100,000 doses distributed. The vaccine-specific serious AEFI reporting rates based on doses distributed were highest for two vaccines given routinely in infancy, Rot-1 and Pneu-C-13 (3.1 and 2.1 per 100,000 doses distributed respectively). Refer to Serious AEFIs for further information.

For annual vaccine-specific reporting rates prior to 2017, see Appendix 2 or the Vaccine Safety Surveillance tool.

Table 1. Number of Reports of AEFIs and AEFI Reporting Rates per 100,000 Doses Distributed by Vaccine: Ontario, 2017

Vaccine[1]	Number of AEFI Reports	Vaccine-Specific Reporting Rate[2]	Number of Serious Reports	Vaccine-Specific Serious Reporting Rate[2]	Doses Distributed[2]
Infant and childhood vaccines					
DTaP-IPV-Hib	75	13.4	11	2.0	560,252
Pneu-C-13	74	15.4	10	2.1	479,383
Rot-1	27	9.2	9	3.1	294,005
Men-C-C	39	21.7	3	1.7	179,654
MMR	62	20.7	5	1.7	299,968
Var	39	18.6	0	0.0	209,329
MMRV	24	12.5	0	0.0	191,774
DTaP-IPV	3	170.8	0	0.0	1,756
Tdap-IPV	33	14.5	2	0.9	227,264
Adolescent vaccines					
HB	56	22.6	1	0.4	247,649
HPV4 and HPV9 combined[3]	76	27.3	1	0.4	278233
HPV4	29	20.2	0	0.0	143,864
HPV9[3]	47	35.0	1	0.7	134,369
Men-C-ACWY	61	32.8	2	1.1	186,258
Tdap	58	7.4	0	0.0	788,773
Routine adult vaccines					

Vaccine[1]	Number of AEFI Reports	Vaccine-Specific Reporting Rate[2]	Number of Serious Reports	Vaccine-Specific Serious Reporting Rate[2]	Doses Distributed[2]
Pneu-P-23	68	30.3	2	0.9	224,506
Td	6	3.1	0	0.0	195,041
Zos	53	40.4	0	0.0	131,045
Universal Influenza Immunization Program (UIIP)					
Inf	167	4.1	5	0.1	4,037,049
Other high-risk publicly-funded, travel, and non-publicly-funded vaccines					
HA	6	-	1	-	-
HAHB	7	-	0	-	-
Men-B	7	-	2	-	-
Rab	3	-	0	-	-
Typh-I	1	-	0	-	-
YF	3	-	1	-	-

AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

Vaccine doses distributed: MOHLTC, Panorama Enhanced Analytical Reporting, extracted by MOHLTC [2018/05/08].

Notes:

1. Only those vaccines with AEFI reports are shown. See Appendix 1 of the Technical Annex for a list of all vaccine abbreviations and corresponding vaccine product/trade names. Vaccines are grouped by main category of recommended age of receipt, as per the *Publicly Funded Immunization Schedules for Ontario – December 2016*.[3]

2. Vaccine-specific reporting rates per 100,000 doses distributed are calculated for routine, publicly-funded vaccines only, due to unknown vaccine distribution for other vaccines within the private market.

3. HPV9 replaced HPV4 for the school-based immunization program in September 2017. For comparison, both the combined and individual vaccine-specific rates are shown.

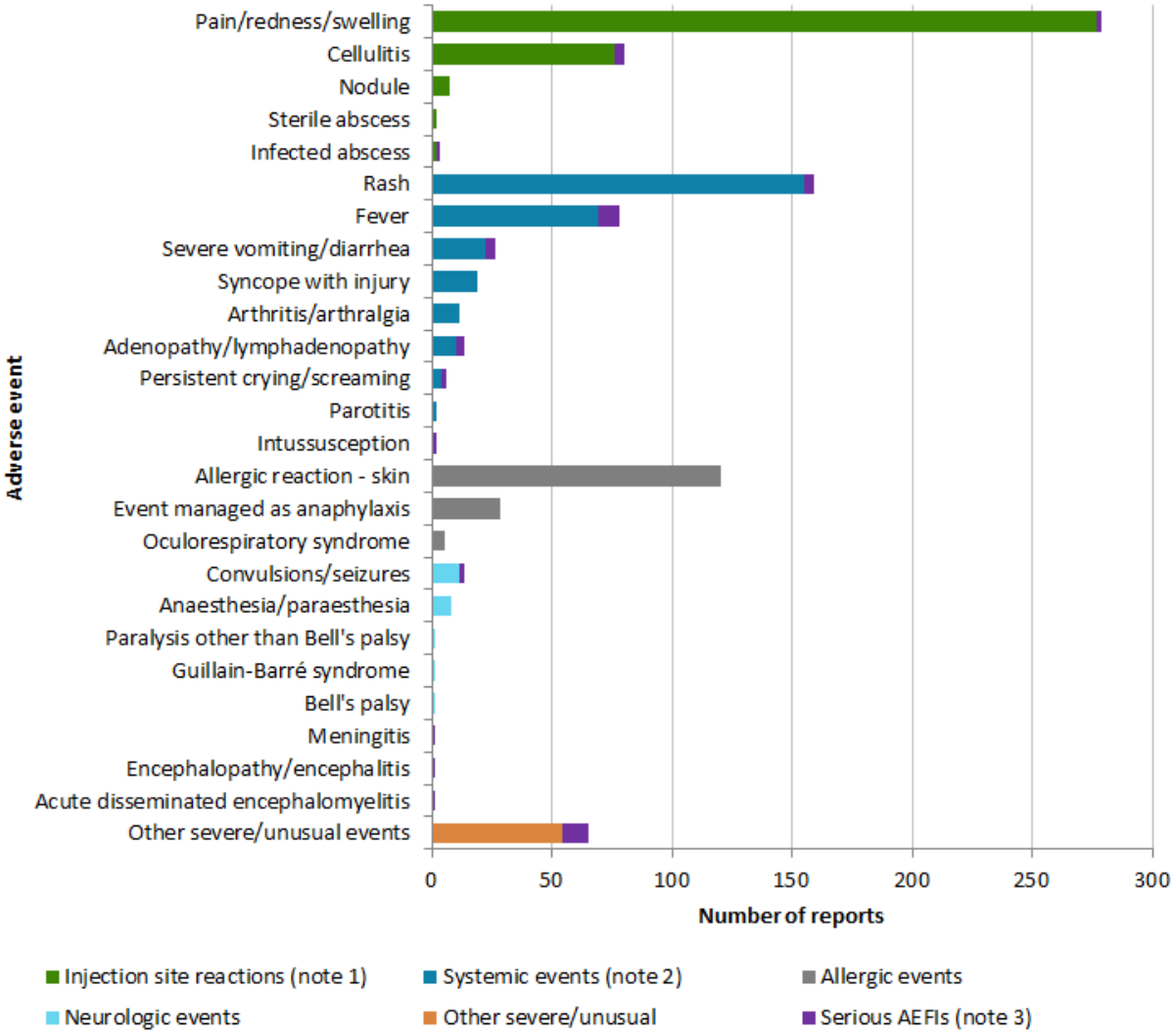
Adverse Event Descriptions

The type of adverse event was recorded in all reports (n=696) in 2017; 96.3% of these were classified as non-serious. The most frequently reported specific adverse event-types were pain, redness or swelling at the injection site, followed by rash and allergic skin reactions (Figure 9).

At least one injection site reaction was recorded in 48.9% (n=340) of all AEFI reports (Table 2) and 98.2% of these were classified as non-serious. Of these 340 reports, injection site reactions were the only reported adverse event-type in 252 reports (74.1%). Routinely administered vaccines that had the highest reporting rates for injection site reactions were Zos and Pneu-P-23 (32.8 and 27.6 per 100,000 doses distributed, respectively).

Rashes were the second most frequently reported specific adverse event-type, present in 22.8% of reports (n=159); 97.5% were classified as non-serious. Among those AEFI reports with rash, 45.3% (n=72) were associated with administration of a live virus vaccines (either MMR, MMRV, Var or Zos) and 62.5% (n=45) of these occurred within five to 42 days of vaccine administration (i.e., within the expected range of time to rash onset for live virus vaccines); the remaining 27 reports (37.5%) indicated a rash occurred within four days or less of vaccine administration. Among those occurring within five to 42 days, four were confirmed as vaccine-strain by genotyping, including three that were measles vaccine strain (all following MMR vaccine, one serious - see further description in Serious AEFIs) and one varicella vaccine strain (following varicella vaccine), which was classified as non-serious. For annual reporting rates by specific adverse event-types prior to 2017, see Appendix 2 or the Vaccine Safety Surveillance tool.

Figure 9. Number of Non-serious and Serious AEFI Reports by Adverse Event-Type and Category: Ontario, 2017



AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

Notes:

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

Table 2. Number and Distribution of AEFI Reports by Adverse Event Category: Ontario, 2017

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[1]	340	48.9	6
Cellulitis	80	11.5	4
Infected abscess	3	0.4	1
Nodule	7	1.0	0
Pain/redness/swelling at the injection site	279	40.1	2
Pain/redness/swelling extending beyond nearest joint	84	12.1	1
Pain/redness/swelling 4-10 days	164	23.6	1
Pain/redness/swelling >10 days	58	8.3	0
Sterile abscess	2	0.3	0
Systemic events[1]	251	36.1	12
Adenopathy/lymphadenopathy	13	1.9	3
Arthritis/arthralgia	11	1.6	0
Fever in conjunction with another reportable event	78	11.2	9
Intussusception[5]	2	0.3	2
Parotitis	2	0.3	0
Persistent crying/screaming	6	0.9	2
Rash	159	22.8	4
Severe vomiting/diarrhea	26	3.7	4
Syncope with injury	19	2.7	0
Allergic events[1]	150	21.6	0

Adverse Event Category[1]/ Adverse Event[2]	Number of AEFI Reports[3]	Percent of All AEFI Reports (%)[4]	Number of Serious AEFI Reports
Allergic reaction – skin	120	17.2	0
Event managed as anaphylaxis[5]	28	4.0	0
Oculorespiratory syndrome (ORS)	5	0.7	0
Neurologic events[1]	27	3.9	5
Acute disseminated encephalomyelitis[5]	1	0.1	1
Anaesthesia/paraesthesia	8	1.1	0
Bell's palsy	1	0.1	0
Convulsions/seizures	13	1.9	2
Encephalopathy/encephalitis[5]	1	0.1	1
Guillian-Barré syndrome[5]	1	0.1	0
Meningitis[5]	1	0.1	1
Paralysis other than Bell's palsy	1	0.1	0
Other severe/unusual events	65	9.3	11

AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

Notes:

1. Adverse event categories represent groupings of specific adverse events within a common category. An AEFI report may contain multiple adverse events from different adverse event categories, as well as more than one adverse event within the same adverse event category. Reports with more than one adverse event within the same category are counted only once in the category totals. Therefore, the sum of adverse event-specific counts within a category may not equal to the category total.

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 Appendix 2 of the Technical Annex.

3. Each AEFI report may contain one or more specific adverse events. Thus the sum will not equal to the total number of AEFIs reported in 2017.

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=696).

5. Classified as medically important events. See Technical Annex for further detail on the definition of medically important events.

There were 34 AEFIs reported that were classified as medically important events in 2017, representing 4.9% of all reports (please see the Technical Annex for a description of a medically important event). Five of these 34 events also met the definition of a serious AEFI and are therefore described under Serious AEFIs, below. Of the remaining 29 medically important events, the majority (n=28) were reports of events managed as anaphylaxis among persons who ranged in age from one to 83 years and one report of Guillian-Barré syndrome in an adult after receiving live zoster vaccine (Zos). Among the 28 anaphylaxis reports, the most frequently reported vaccines were Inf (n=13), Men-C-ACYW (n=4), DTaP-IPV-Hib (n=3) and HPV-9 (n=3).

The overall reporting rate of anaphylaxis within publicly-funded vaccine programs in 2017 was 3.3 per 1,000,000 doses distributed; this represents an increase after a period of decline between 2012 and 2016 (from 2.5 to 1.2 per 1,000,000 doses distributed). All 28 reports were assessed using the Brighton Collaboration standard definition of anaphylaxis.[4] Fifteen met the Brighton definition, seven at level I of diagnostic certainty, seven at level II and one at level III, for a corresponding reporting rate of 1.8 per 1,000,000 doses distributed. The remaining 13 (46.4%) reports did not have sufficient documented evidence to meet levels I, II or III of diagnostic certainty of the Brighton anaphylaxis case definition. The proportion of anaphylaxis reports that met the Brighton definition decreased in 2017 to 53.6% (15/28) compared to 80.0% (8/10) the previous year. None of the anaphylaxis reports were classified as serious.

Serious AEFIs

There were 26 AEFI reports in 2017 that were classified as serious (please see the Technical Annex for a description of a serious AEFI), representing 3.7% (26/696) of all reports and a serious AEFI reporting rate of 1.8 per 1,000,000 population. There were 25 serious AEFI reports following administration of at least one publicly-funded vaccine (2.9 per 1,000,000 publicly-funded doses distributed). The majority of serious AEFIs (73.1%; n=19) occurred in individuals under 18 years of age, with most in children under four years (n=16). Of the 25 serious AEFIs in 2017 that were admitted to hospital, the mean length of stay was 10 days. There were 10 serious AEFIs that were documented as being reported by IMPACT (Immunization Monitoring Program ACTive)[1], ranging in age from two months to three years. The

[1] IMPACT is Canada's Immunization Monitoring Program ACTive and 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.

proportion of AEFIs defined as serious remained relatively stable between 2012 and 2015 (range: 4.0% to 5.0%), but decreased in 2016 and 2017 (3.3% and 3.7%, respectively).

Serious AEFIs were summarized further based on case-level review. Among 26 serious AEFIs, there were a total of eight reports of febrile illness including seven that were in children under four years of age. Descriptions of febrile illness included three diagnosed with Kawasaki disease (KD) and one each of pneumonia, febrile seizure, severe vomiting and diarrhea, laboratory-confirmed measles vaccine strain illness, and management of fever requiring hospitalization due to an underlying medical condition. Of the remaining serious AEFIs, four were injection site reactions (three cellulitis and one infected abscess), four neurological events (one each of encephalopathy, aseptic meningitis, acute disseminated encephalomyelitis [ADEM] and a transient ischemic attack), two reports of intussusception, two reports of respiratory distress and one each of seizure (non-febrile), gastroesophageal reflux disease (GERD)/poor oral feeding, vaso-occlusive crisis, persistent vomiting with low hemoglobin and vasculitis. In addition, there was one reported death in 2017. The report was of sudden death in a one year old occurring within 24 hours of receipt of DTaP-IPV-Hib. A coroner's investigation for this case found the cause of death was 'unascertained'; however, there were possible natural causes identified that were likely to have a significant contribution to the death. For more information about specific serious AEFI reports, please see Appendix 4.

Healthcare Utilization and Outcome

Among those AEFI reports with the corresponding healthcare utilization fields completed in iPHIS, 75.5% (524/694) sought out-patient medical consultation, 38.0% (167/439) had an emergency room visit and 3.9% (27/694) indicated a hospitalization had occurred (this included two reports with admission and discharge dates on the same day which precluded them from classification as a serious AEFI).

In terms of AEFI outcomes, the majority of individuals had recovered at the time of assessment (70.7%), followed by those who were not yet recovered, but likely to recover (22.1%). In a small proportion of reports (2.9%; n=20), the outcome was reported as "residual effects," which is defined as residual disability or sequelae related to the reported event. Due to the relatively short follow-up time for AEFIs reported in iPHIS, it is uncertain whether these residual effects represent long-term residual disability or events which will resolve, but had not yet resolved at the time of reporting. In addition, there was one report of death in 2017, which is described in the Serious AEFI section above.

Risk Factors

The three medical risk factors that are collected for provincial AEFI surveillance (i.e., required in iPHIS) are: chronic illness/underlying medical condition, immunocompromised and immunization program error. Among all AEFI reports in 2017, 140 (20.1% of all AEFIs) reported an affirmative response to at least one of the three above-named risk factors. Of these, 93.6% (n=131) reported having a chronic illness/underlying medical condition, 2.9% (n=4) reported being immunocompromised and 7.9% (n=11) reported an immunization program error. Among immunization program errors, eight were related to administration errors (e.g., incorrect land-marking and wrong route of administration), two were the

result of non-adherence to vaccine indications or recommendations for use and in one case the wrong immunizing agent was administered (Menjugate® was given instead of Menactra®).

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

Overall, we found a low rate of AEFI reporting in Ontario following vaccines administered in 2017 and no unexpected vaccine safety issues.

The provincial AEFI reporting rate increased slightly in 2017 (4.9 per 100,000 population) compared to previously published 2016 data (4.5 per 100,000 population). Typically, changes in AEFI reporting associated with the infant and childhood schedule will affect the overall reporting rate due to the large volume of reports received for this group. In 2017, we observed increases in both the one to three year old and four to 10 year old reporting rates, while there were decreases in the <1 year old and 11 to 17 year old reporting rates. Additionally, an increase in AEFI reporting is also expected following introduction of new vaccines or new populations in the publicly-funded immunization program. There have been three recent changes in Ontario that may affect the AEFI reporting rate, namely Zos, HPV9 and expansion of the HPV immunization program to males.

Ontario's AEFI reporting rate has been consistently lower relative to other jurisdictions. Some differences in rates are expected across different geographic areas due to variability in reporting requirements, case definitions, immunization programs and population demographic characteristics. As a comparison, the Canadian national AEFI reporting rate was 11.9 per 100,000 doses in 2017[5] and the Australian annual reporting rate was 12.3 per 100,000 population in 2015.[6] The causes of Ontario's low reporting rate are likely multifactorial, including under-reporting by healthcare providers; [7-9] which is discussed in further detail in previous reports.[10-14] The World Health Organization[15] has introduced the concept of a benchmark for reporting rates among infants and suggests a value of 10 reports per 100,000 surviving infants should be used.

Similar to previous years, wide variation in population-based AEFI reporting by PHUs for both infant and early childhood vaccine programs, school-based programs and influenza was observed in 2017. The high geographic variability in AEFI reporting rates may in part be related to variability in the interpretation and promotion of AEFI reporting among local health care providers within jurisdictions and different reporting processes for AEFIs across PHUs, all of which drives provincial AEFI reporting; however, fewer PHUs reported zero AEFIs in 2017 in all of the three categories which comprise the majority of vaccine doses distributed for the publicly-funded program in the province combined (routine infant and early childhood vaccines, school-based vaccines and influenza vaccine), compared to 2016 (two versus six PHUs, respectively).

Limitations in population-based reporting rates relative to reporting rates using a dose distribution denominator have previously been described.[14] In the absence of a population-based provincial immunization registry which would allow for an accurate assessment of the number of doses administered to individuals residing in each area, doses distributed data serves as a proxy and enables a more accurate comparison of AEFI reporting rates across geographic areas by taking into account the differences in vaccine distribution relative to population-based reporting rates.

As with previous years, the population-based rate of AEFI reporting was highest in the youngest age groups. This is expected as most routine vaccine series are administered to infants and young children.[3] In 2017, the reporting rate for infants under one year of age declined slightly in 2017 in comparison to larger fluctuations in reporting rate between 2012 and 2016. Among children aged one to three years, a slight increase was observed. There were no immunization program changes in 2017 to account for the variation in reporting rates in these two age groups. In contrast, the introduction of the publicly-funded Zos program among adults 65-70 years old did not appear to impact the age-specific rate for those 65 years and older. This may be due to the fact that Zos doses were available for private purchase for several years prior to the introduction of the publicly-funded program. Similarly, the first full year of the expanded HPV program to include males did not appear to impact the age-specific rate for the 11 to 17-year-old age group; however, among adolescents 11-to 17-years old, the female to male ratio declined slightly in 2017 relative to 2016 (1.7 in 2016 and 1.5 in 2017), likely due to the expansion of the publicly-funded HPV vaccination program to grade seven males in September 2016. In general, there is a female predominance in AEFI reports, particularly among adults and this is consistently observed in Ontario,[16] as well as in other passive AEFI surveillance systems.[17,18]

Vaccine-specific reporting rates in 2017 were highest for Zos, HPV9 and Men-C-ACYW using doses distributed in the denominator, although serious reporting rates for all three vaccines were low. For Zos, the higher reporting rate is not unexpected given the known reactogenicity of this vaccine.[19,20] HPV9 and Men-C-ACYW are two vaccines primarily delivered by PHUs within school-based programs where higher AEFI reporting is typically observed compared to program delivery by other providers.[10-14] In addition, local adverse events are more common following HPV9 compared to HPV4 (HPV9 replaced HPV4 in September 2017). [21] This product change, in addition to being the first full year for the publicly-funded program for boys, may have contributed towards the increase in reporting rates for HPV9 in 2017.

As in previous years, mild events (e.g., injection site reactions and rash) were the most frequently reported reactions. This is expected based on the safety profile of many vaccines and is consistently observed in AEFI surveillance systems in other jurisdictions.[17,18] There were no notable trends in the reporting of specific types of medically important events with the exception of anaphylaxis, where the number and rate of reports of events managed as anaphylaxis increased in 2017 compared to the last five years. Further assessment of these reports demonstrated that they were associated with various vaccines and age groups; no specific clustering or vaccine-specific signal was observed. It is important to note that the surveillance criteria for reporting an AEFI as anaphylaxis in Ontario includes all events managed as anaphylaxis (e.g., epinephrine administered). This definition is deliberately sensitive to ensure that cases of potential anaphylaxis in Ontario undergo further assessment. Despite the increase, the reporting rate of anaphylaxis in 2017 (3.3 per million doses) is still within the range of expected rates, which is between one and 10 episodes per million vaccine doses administered.[22]

The relatively low proportion of anaphylaxis reports that met the Brighton definition (54.0%) compared to previous years highlights the importance of applying Brighton definition case level review at the provincial level to assess reported events. Implementation of the anaphylaxis case report form in 2014 led to improvements in data quality; however, ongoing assessment can help to further understand and interpret reports of anaphylaxis in the context of AEFI surveillance including the role of surveillance

reporting criteria, standard case definitions and variations in health care provider management and subsequent reporting of these events. Anaphylaxis is a life-threatening emergency and all immunizing providers should be able to assess and promptly treat anaphylaxis with epinephrine.[22]

Serious AEFIs were very rarely reported in 2017. The rate of serious AEFIs was slightly higher than last year; however, this increase is in keeping with the slight increase in the overall AEFI reporting rate this year. The types of serious AEFIs reported were most often related to rare events that are known to be reported following vaccination. For example, there was one report of ADEM in an adult following receipt of influenza vaccine in which the individual was noted to have residual effects. ADEM is an acute, often rapidly progressing autoimmune disease of the central nervous system. It is commonly triggered by an infection, but has also been shown to occur following vaccination, although the mechanism of disease is not completely understood.[23] Using data from the U.S. vaccine safety reporting system, one study[24] estimated the incidence of ADEM after vaccination against influenza to be 0.05 per million doses. Since 2012, there has only been one other report of ADEM in Ontario, a non-serious AEFI reported in 2013 in an elderly individual following receipt of zoster vaccine, where the individual was subsequently diagnosed with new onset multiple sclerosis. Causality assessments have found insufficient evidence to accept or reject a causal association between ADEM and influenza vaccine, as well as a number of other vaccines.[25] Additionally, we had one report of encephalitis following YF + Inf vaccine in 2017 in an adult who had not yet recovered at the time of reporting. Yellow fever vaccine-associated neurologic disease has been previously described in the annual safety report following a report of this event in 2014.[12]

The reported death of a one year old following receipt of routine vaccines was subject to a Coroner's investigation and is being reviewed by the Pediatric Deaths Under Five Committee of the Office of the Chief Coroner of Ontario, with final results pending. While there was an unascertained cause of death, there were possible natural causes identified during autopsy that likely had a significant contribution to the death. Further details on the definition of an unascertained cause of death and the provincial AEFI reporting of fatal events can be found in the 2013 PHO Vaccine Safety Report.[11]

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

Conclusions

This report summarizes AEFIs reported in Ontario following vaccines administered in 2017, as well as reporting trends since 2012. Overall, a low rate of AEFI reporting continued to be observed in the province, though a wide range in reported AEFI rates was found among PHUs, as well as some improvements in reporting rates by PHUs compared to 2016. No unexpected vaccine safety issues were identified – the most commonly reported events were mild (e.g., injection site reactions); further analysis is needed to explore reasons for the higher number of anaphylaxis reports observed in 2017 with the lower proportion of those reports meeting Brighton definitions. Serious events were very rare and the majority of individuals had recovered at the time of reporting. Ongoing surveillance of AEFIs in Ontario is needed to monitor vaccine safety and to assess and interpret trends within the context of changes to provincial immunization programs, with the goal of improving reporting within the surveillance system.

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Appendix 1: Number of AEFI Reports and Reporting Rates of AEFIs by Public Health Unit: Ontario, 2017

Public Health Unit	Number of AEFI Reports	Population	Reporting Rate per 100,000 Population
Ontario	696	14,229,571	4.9
Northwestern Health Unit	18	81,752	22.0
Eastern Ontario Health Unit	39	207,381	18.8
Timiskaming Health Unit	5	33,543	14.9
Kingston, Frontenac, Lennox & Addington Public Health	26	206,548	12.6
North Bay Parry Sound District Health Unit	14	128,404	10.9
Oxford County Public Health	12	113,252	10.6
Durham Region Health Department	71	682,151	10.4
Simcoe Muskoka District Health Unit	55	566,423	9.7
Leeds, Grenville and Lanark District Health Unit	16	170,000	9.4
Haliburton, Kawartha, Pine Ridge District Health Unit	15	183,331	8.2
Peterborough County-City Health Unit	11	142,510	7.7
Perth District Health Unit	6	79,169	7.6
Sudbury & Diustrict Health Unit	15	199,811	7.5
Huron County Health Unit	4	59,113	6.8
Grey Bruce Health Unit	11	165,405	6.7
Elgin-St. Thomas Public Health	6	91,718	6.5

Public Health Unit	Number of AEFI Reports	Population	Reporting Rate per 100,000 Population
Region of Waterloo Public Health	36	557,446	6.5
Algoma Public Health	7	115,027	6.1
Hastings Prince Edward Public Health	10	164,577	6.1
City of Hamilton Public Health Services	34	569,908	6.0
Windsor-Essex County Health Unit	23	412,432	5.6
Wellington-Dufferin-Guelph Public Health	16	295,018	5.4
Ottawa Public Health	48	996,651	4.8
Brant County Health Unit	7	149,249	4.7
Halton Region Health Department	22	582,683	3.8
Porcupine Health Unit	3	85,157	3.5
Peel Public Health	51	1,507,069	3.4
Lambton Public Health	4	129,960	3.1
Chatham-Kent Public Health	3	105,392	2.8
Renfrew County & District Health Unit	3	107,236	2.8
Thunder Bay District Health Unit	4	153,988	2.6
Toronto Public Health	73	2,952,051	2.5
Niagara Region Public Health	9	458,615	2.0
York Region Public Health	17	1,180,629	1.4
Middlesex-London Health Unit	2	484,354	0.4
Haldimand-Norfolk	0	111,618	0.0

AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

Population: IntelliHEALTH Ontario[2]

Appendix 2: Number of AEFI Reports and Reporting Rates of AEFIs by Vaccine: Ontario, 2012-17

Vaccine[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016	2017	2017
	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]
Infant and childhood vaccines												
DTaP-IPV-Hib	63	11.2	75	13.3	55	9.7	53	9.3	72	12.5	75	13.4
Pneu-C-13	49	11.0	57	13.0	54	12.5	60	12.9	51	10.7	74	15.4
Rot-1	24	9.8	26	9.9	21	8.1	18	6.7	25	9.4	27	9.2
Men-C-C	16	10.3	22	14.8	26	16.2	40	20.0	24	11.5	39	21.7
MMR	38	13.2	48	15.9	50	18.4	74	21.6	39	14.2	62	20.7
Var	59	15.9	61	20.1	54	20.5	58	22.1	56	25.3	39	18.6
MMRV	4	14.1	4	14.1	1	1.0	16	10.0	19	10.9	24	12.5
DTaP-IPV	54	105.9	8	340.4	13	N/A	1	18.0	0	0.0	3	170.8
Tdap-IPV	13	9.0	27	13.0	8	3.8	30	12.3	28	11.6	33	14.5

Vaccine[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016	2017	2017
	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]
Adolescent vaccines												
Men-C-ACWY	25	21.2	43	36.0	42	25.9	60	36.5	42	23.0	61	32.8
HB	58	24.5	67	25.0	47	17.5	56	22.2	73	28.5	56	22.6
HPV4	49	28.4	47	26.4	39	24.4	42	29.5	83	39.6	29	20.2
HPV9[3]	N/A	N/A	N/A	N/A	N/A	N/A	4	N/A	5	N/A	47	35.0
Tdap	60	9.0	56	8.3	75	11.9	85	10.8	66	8.2	58	7.4
Routine adult vaccines												
Pneu-P-23	42	20.6	59	25.1	35	14.5	63	23.1	67	28.2	68	30.3
Td	11	3.5	13	4.7	6	2.2	6	2.4	7	3.4	6	3.1
Td-IPV	1	4.1	0	0.0	0	0.0	1	5.1	0	0.0	0	0.0
Zos[4]	31	N/A	42	N/A	41	N/A	59	N/A	54	N/A	53	40.4
Universal Influenza Immunization Program (UIIP)												
Inf	198	5.3	190	4.5	153	3.4	167	3.7	129	3.6	167	4.2
Other high-risk publicly-funded, travel, and non-publicly-funded vaccines												

Vaccine[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016	2017	2017
	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]
BCG	1	-	0	-	0	-	0	-	0	-	0	-
Chol-Ecol-O	1	-	1	-	1	-	1	-	0	-	0	-
Chol-O	0	-	1	-	0	-	0	-	0	-	0	-
HA	3	-	2	-	3	-	5	-	5	-	6	-
HAHB	10	-	7	-	17	-	16	-	8	-	7	-
HA-Typh-I	3	-	5	-	0	-	1	-	1	-	0	-
Hib	0	-	3	-	0	-	0	-	0	-	0	-
HPV2	1	-	1	-	0	-	0	-	0	-	0	-
IPV	3	-	0	-	1	-	1	-	1	-	0	-
JE	1	-	0	-	0	-	0	-	0	-	0	-
Men-B	N/A	-	0	-	3	-	3	-	10	-	7	-
Rab	6	-	7	-	6	-	2	-	6	-	3	-
Typh-I	6	-	1	-	3	-	2	-	1	-	1	-
Typh-O	2	-	1	-	1	-	0	-	0	-	0	-

Vaccine[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016	2017	2017
	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]	Number of AEFI Reports	Reporting Rate[2]
YF	8	-	7	-	5	-	4	-	3	-	3	-
Total AEFIs[5]	688		695		601		717		670		696	

AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

Vaccine doses distributed: MOHLTC, Panorama Enhanced Analytical Reporting, extracted by MOHLTC [2018/05/08].

Notes:

1. Only those vaccines with AEFI reports are shown. See Appendix 1 of the Technical Annex for a list of all vaccine abbreviations and corresponding vaccine product/trade names. Vaccines are grouped by recommended age of receipt as per the *Publicly Funded Immunization Schedules for Ontario – December 2016*.[3] Recommended age of receipt may vary for some vaccines, as it depends on the immunization status of individuals and vaccine-specific indications.
2. Vaccine-specific reporting rates per 100,000 doses distributed are calculated for routine, publicly-funded vaccines only, due to unknown vaccine distribution for other vaccines within the private market.
3. HPV9 replaced HPV4 for the school-based immunization program in September 2017; reporting rates are provided as of this date.
4. Zos was added to the publicly-funded program in September 2016; reporting rates are provided as of 2017.
5. As each AEFI report may be associated with one or more vaccine, the sum of vaccine-specific AEFI reports may not equal to the total number of AEFIs reported each year.

Appendix 3: Number of AEFI Reports and Percent of AEFIs by Adverse Event-Type and Category: Ontario, 2012-17

Adverse Event Category[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016	2017	2017
Adverse Event[2]	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**
Injection site reactions[1]	278	40.4	283	40.7	264	43.9	309	43.1	323	48.2	340	48.9
Cellulitis	60	8.7	64	9.2	48	8.0	72	10.0	71	10.6	80	11.5
Infected abscess	4	0.6	6	0.9	2	0.3	1	0.1	4	0.6	3	0.4
Nodule	23	3.3	11	1.6	14	2.3	8	1.1	8	1.2	7	1.0
Pain/redness/swelling at the injection site[1]	211	30.7	232	33.4	216	35.9	250	34.9	263	39.3	279	40.1
Pain/redness/swelling extending beyond nearest joint	18	2.6	58	8.3	70	11.6	59	8.2	84	12.5	84	12.1
Pain/redness/swelling <4 days[3]	61	8.9	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Pain/redness/swelling ≥4 days[3]	63	9.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Pain/redness/swelling 4-10	62	9.0	155	22.3	131	21.8	160	22.3	168	25.1	164	23.6

Adverse Event Category[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016	2017	2017
Adverse Event[2]	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**
days[4]												
Pain/redness/swelling >10 days[4]	22	3.2	39	5.6	36	6.0	54	7.5	37	5.5	58	8.3
Sterile abscess	7	1.0	0	0.0	5	0.8	1	0.1	2	0.3	2	0.3
Systemic events[1]	206	29.9	258	37.1	221	36.8	291	40.6	249	37.2	251	36.1
Adenopathy/ lymphadenopathy	5	0.7	10	1.4	8	1.3	10	1.4	12	1.8	13	1.9
Arthritis/arthralgia	11	1.6	14	2.0	15	2.5	16	2.2	11	1.6	11	1.6
Fever in conjunction with another reportable event	57	8.3	62	8.9	73	12.1	92	12.8	68	10.1	78	11.2
Hypotonic-hyporesponsive episode (HHE)	5	0.7	3	0.4	7	1.2	3	0.4	4	0.6	0	0.0
Intussusception[5]	0	0.0	1	0.1	0	0.0	3	0.4	2	0.3	2	0.3
Parotitis	2	0.3	1	0.1	0	0.0	2	0.3	1	0.1	2	0.3
Persistent crying/screaming	6	0.9	6	0.9	7	1.2	3	0.4	6	0.9	6	0.9
Rash	150	21.8	156	22.4	129	21.5	176	24.5	151	22.5	159	22.8

Adverse Event Category[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016	2017	2017
Adverse Event[2]	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**
Severe vomiting/diarrhea[4]	6	0.9	35	5.0	28	4.7	34	4.7	29	4.3	26	3.7
Syncope with injury[4]	0	0.0	6	0.9	11	1.8	18	2.5	14	2.1	19	2.7
Thrombocytopenia[5]	0	0.0	2	0.3	0	0.0	1	0.1	3	0.4	0	0.0
Allergic events[1]	171	24.9	144	20.7	116	19.3	145	20.2	124	18.5	150	21.6
Allergic reaction – other[3]	16	2.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Allergic reaction – skin	135	19.6	131	18.8	98	16.3	126	17.6	113	16.9	120	17.2
Event managed as anaphylaxis[5]	20	2.9	17	2.4	12	2.0	16	2.2	10	1.5	28	4.0
Oculorespiratory syndrome (ORS)	6	0.9	1	0.1	6	1.0	7	1.0	3	0.4	5	0.7
Neurologic events[1]	32	4.7	36	5.2	24	4.0	40	5.6	24	3.6	27	3.9
Acute disseminated encephalomyelitis [5]	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1
Anaesthesia/paraesthesia[4]	7	1.0	15	2.2	7	1.2	18	2.5	13	1.9	8	1.1
Bell's palsy	3	0.4	2	0.3	2	0.3	6	0.8	2	0.3	1	0.1
Convulsions/seizures	15	2.2	14	2.0	11	1.8	12	1.7	7	1.0	13	1.9

Adverse Event Category[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016	2017	2017
Adverse Event[2]	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**	**Number of AEFI Reports**	**%[7]**
Encephalopathy/ encephalitis[5]	2	0.3	1	0.1	0	0.0	0	0.0	1	0.1	1	0.1
Guillian-Barré syndrome[5]	2	0.3	2	0.3	1	0.2	3	0.4	1	0.1	1	0.1
Meningitis[5]	0	0.0	1	0.1	2	0.3	2	0.3	0	0.0	1	0.1
Myelitis[5]	0	0.0	0	0.0	0	0.0	2	0.3	1	0.1	0	0.0
Paralysis other than Bell's palsy	3	0.4	1	0.1	2	0.3	0	0.0	0	0.0	1	0.1
Other severe/ unusual events[1]	143	20.8	99	14.2	85	14.1	82	11.4	61	9.1	65	9.3
Total AEFIs[6]	688		695		601		717		670		696	

AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2017/05/09].

Notes:

1. Adverse event categories represent groupings of specific adverse events within a common category. An AEFI report may contain multiple adverse events from different adverse event categories, as well as more than one adverse event within the same adverse event category. Reports with more than one adverse event within the same category are counted only once in the category totals. Therefore, the sum of adverse event-specific counts within a category may not equal to the category total.

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 Appendix 2 of the 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. Classified as medically important events. Please refer to Technical Annex for further detail on the definition of medically important events.
6. The total number of confirmed AEFI reports with at least one adverse event reported. As each AEFI report may contain one or more specific adverse events, the sum of event-specific AEFI reports may not equal to the total number of AEFIs reported each year.
7. The denominator is the total number of confirmed AEFI reports with at least one adverse event reported. Percentages will not sum to 100%.

Appendix 4: Summary of Serious AEFIs, 2017

Event-Type[1]	Number of AEFI Reports	Age Group (years)	Associated Vaccines[2]	Additional Information
Febrile illness	8	<1 (n=2) 1-3 (n=5) 18-64 (n=1)	DTaP-IPV-Hib, HA, Inf, Men-B, Men-C-C, MMR, Pneu-C-13, Pneu-P, Rot-1	Three Kawasaki disease (KD) and one each of pneumonia, febrile seizure, seizure vomiting and diarrhea, laboratory-confirmed measles vaccine strain illness, and management of fever requiring hospitalization due to an underlying medical condition.
Local reaction	4	4-10 (n=1) 18-64 (n=2) 65+ (n=1)	HB, Inf, Men-C-ACWY, Pneu-P	Three cellulitis and one infected abscess.
Neurological events	4	11-17 (n=1) 18-64 (n=3)	HPV-9, Inf, Men-C-ACWY, MMR, Tdap-IPV, YF	One each of encephalopathy, aseptic meningitis, acute disseminated encephalomyelitis and transient ischemic attack.
Intussusception	2	<1(n=2)	DTaP-IPV-Hib, Pneu-C-13, Rot-1	-
Respiratory distress	2	<1 (n=2)	DTaP-IPV-Hib, Penu-C-13, Rot-1	-
Seizure	1	<1	DTaP-IPV-Hib, Pneu-C-13, Rot-1	-
GERD/poor oral feeding	1	<1	DTaP-IPV-Hib, Men-B, Pneu-C-13, Rot-1	-

Event-Type[1]	Number of AEFI Reports	Age Group (years)	Associated Vaccines[2]	Additional Information
Vaso-occlusive crisis	1	11-17	Men-C-C, MMR, Tdap-IPV	Onset of chest and thigh pain seven days after receiving vaccine.
Persistent vomiting/low hemoglobin	1	<1	DTap-IPV-Hib, Pneu-C-13, Rot-1	-
Henoch-Schonlein Purpura (HSP)	1	1-3	DTap-IPV-Hib, (Tetanus Ig)	Onset of pupura, upper resipratory tract infection symptoms, arthralgia and ear and abdominal pain approximately two weeks after receiving vaccine.
Sudden death	1	1-3	DTap-IPV-Hib	Occurred within 24 hours of receiving routine immunization. Possible natural causes identified on autopsy.

AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2018/05/11].

Notes:

1. This information is derived from case-level review of all information entered in iPHIS and not necessarily the selected “adverse event reaction(s)” entered into iPHIS.
2. Includes vaccines that were co-administered.

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