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Annual Report on Vaccine Safety in Ontario, 2016

Surveillance Report

November 2017

Public Health Ontario

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Authors

Chi Yon Seo, MSc
Epidemiologist Lead
Immunization and Vaccine-Preventable Diseases
Public Health Ontario

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

Kelty Hillier, MSc
Epidemiologist
Immunization and Vaccine-Preventable Diseases
Public Health Ontario

Tara Harris, RN, MHSc
Manager (A)
Immunization and Vaccine-Preventable Diseases
Public Health Ontario

Jody Stapleton, RN, BHSc, BScN, MIPH
Nurse Consultant
Immunization and Vaccine-Preventable Diseases
Public Health Ontario

Shelley L. Deeks, MD, MHSc, FRCPC, FAFPHM
Chief
Communicable Diseases, Emergency Preparedness and Response
Public Health Ontario

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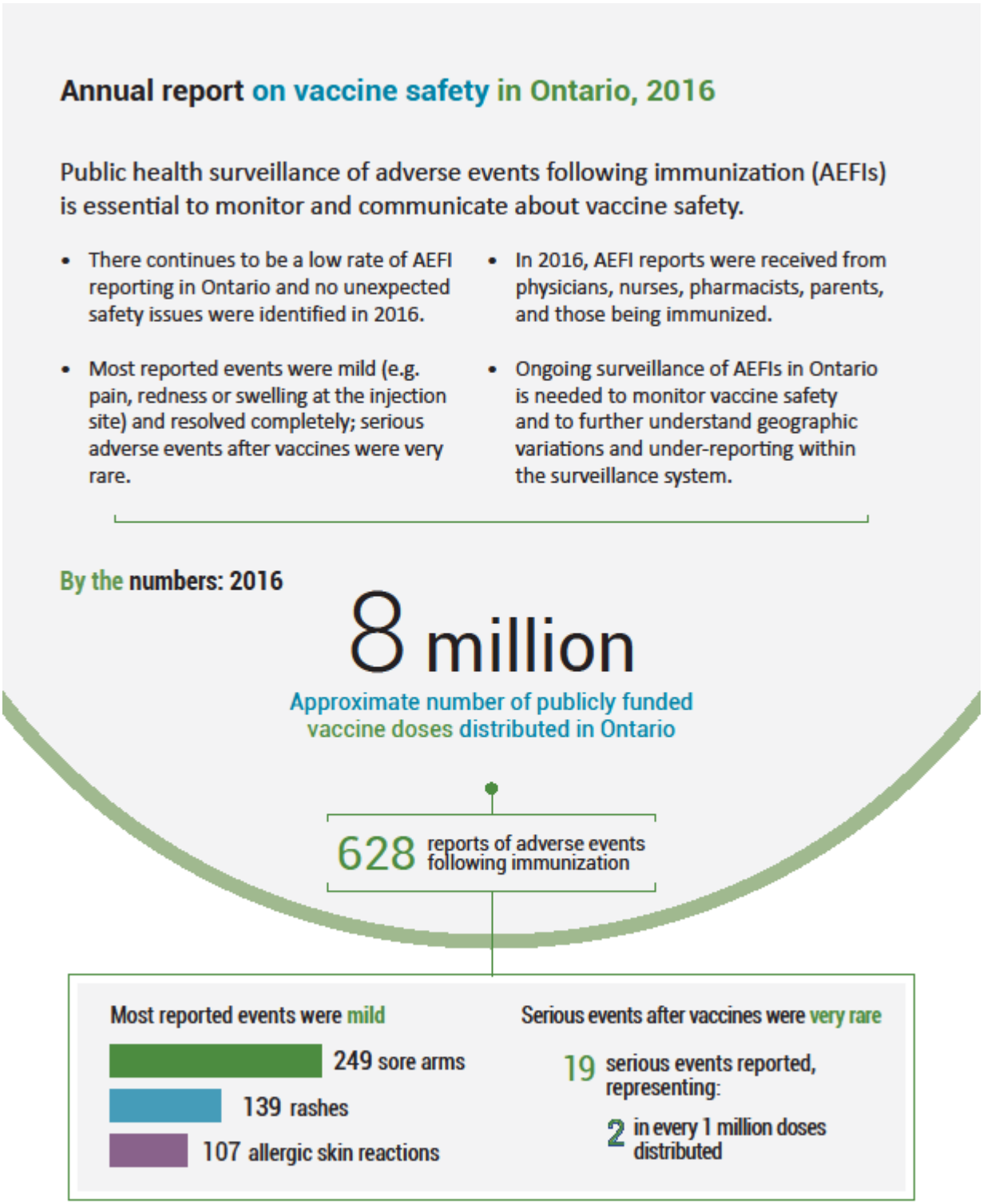
Contents

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 2016, PHO undertook an evaluation to assess whether the Annual Report on Vaccine Safety in Ontario 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. One of the recommendations received from this evaluation was to provide a mechanism for stakeholders to readily access the data presented in the report. As a result, PHO launched the Vaccine Safety Surveillance tool in 2017, an interactive online tool allowing users to explore, manipulate and download vaccine safety data. The data presented in this online tool will be updated each year to include provincial AEFI surveillance data from the previous calendar year and will be released at the same time as the Annual Report on Vaccine Safety in Ontario.

Report objectives and scope

The objective of this report is to summarize AEFIs reported in Ontario following vaccines administered in 2016. In addition, reporting trends are assessed by comparing AEFIs reported in Ontario following vaccines administered across five years between 2012 and 2016.

Methods

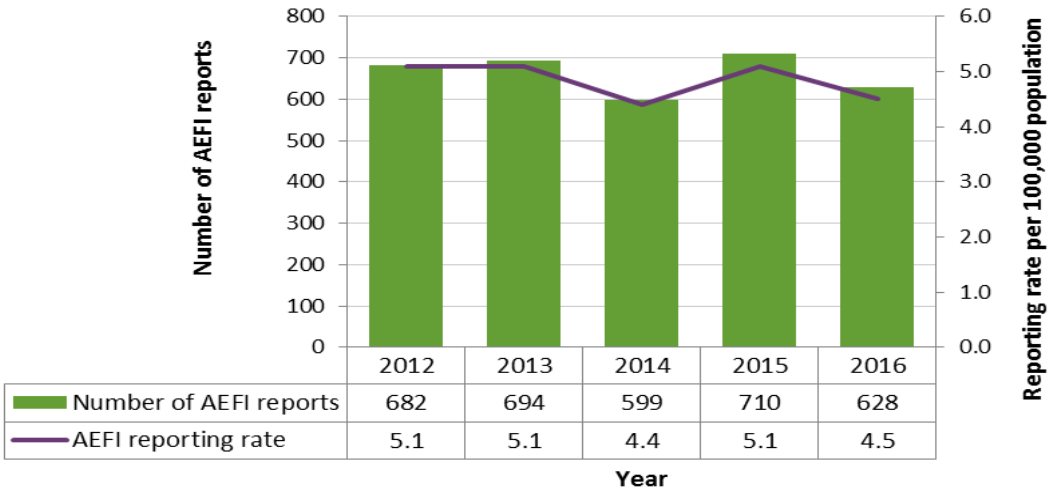
An AEFI report refers to a report received by the PHU which pertains to one individual vaccine recipient who experiences one or more adverse events that are temporally associated (i.e., the event occurs *after* administration of the vaccine) with receipt of one or more vaccines administered at the same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

For a detailed description of the provincial AEFI surveillance system and methods for the analysis of AEFI surveillance data, please see the Technical Annex. The Technical Annex includes details 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 many factors, including changes to the publicly funded immunization program. See Appendix 3 of the Technical Annex for a description of immunization program changes in recent years and Appendix 1 of the Technical Annex for a complete list of vaccine acronyms used in this report.

Results

In Ontario, 628 AEFI reports were received following vaccines administered in 2016, representing a population-based reporting rate of 4.5 per 100,000 population (Figure 1). The annual reporting rate between 2012 and 2016 ranged from 4.4 to 5.1 per 100,000 population with no statistically significant change in trends observed over this five-year period. This 2016 report includes delayed reports received since the data were extracted for the 2015 Annual Report on Vaccine Safety in Ontario (i.e., reports received between May 1, 2016 and May 9, 2017). These accounted for a 0.7%, 0.4%, 1.2% and 4.7% increase of the total number of confirmed AEFI reports in 2012, 2013, 2014 and 2015 respectively, compared to the numbers reported in the 2015 report.

FIGURE 1. NUMBER OF REPORTS AND REPORTING RATE OF AEFIS PER 100,000 POPULATION BY YEAR: ONTARIO, 2012-16



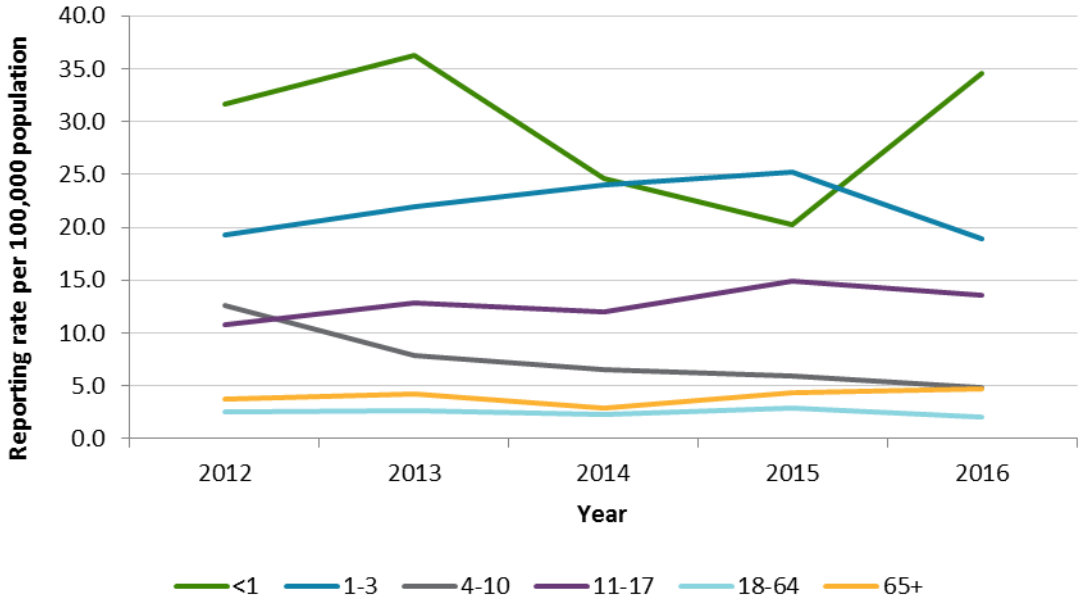
AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2017/05/09].
Population: Population Estimates [2012-15] and Projections [2016], Ontario Ministry of Health and Long-Term Care, IntelliHEALTH ONTARIO, extracted [2016/09/02].
Note: Only includes AEFI reports 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 2016, persons with AEFI reports ranged in age from one month to 91 years, with a median age of 15 years. There was a slight majority of AEFI reports in children and adolescents (under 18 years of age) compared to adults 18 years of age and older (52.4% vs. 47.6% of total AEFI reports, respectively).

Among specific age categories, the highest AEFI reporting rate in 2016 was in infants under one year (34.5 per 100,000 population), followed by children aged one to three years (18.9 per 100,000 population) (Figure 2). The annual age-specific reporting rate for infants under one year increased in 2016, following a decrease observed between 2013 and 2015. Conversely, the annual reporting rate for 1- to 3-year-olds decreased in 2016 after a steady increase between 2012 and 2015. Over the five-year period, the annual age-specific reporting rate for 4- to 10-year-olds has decreased while the rate for 11- to 17-year-olds increased slightly. The reporting rate for adults 18 years of age and over has remained low and relatively stable.

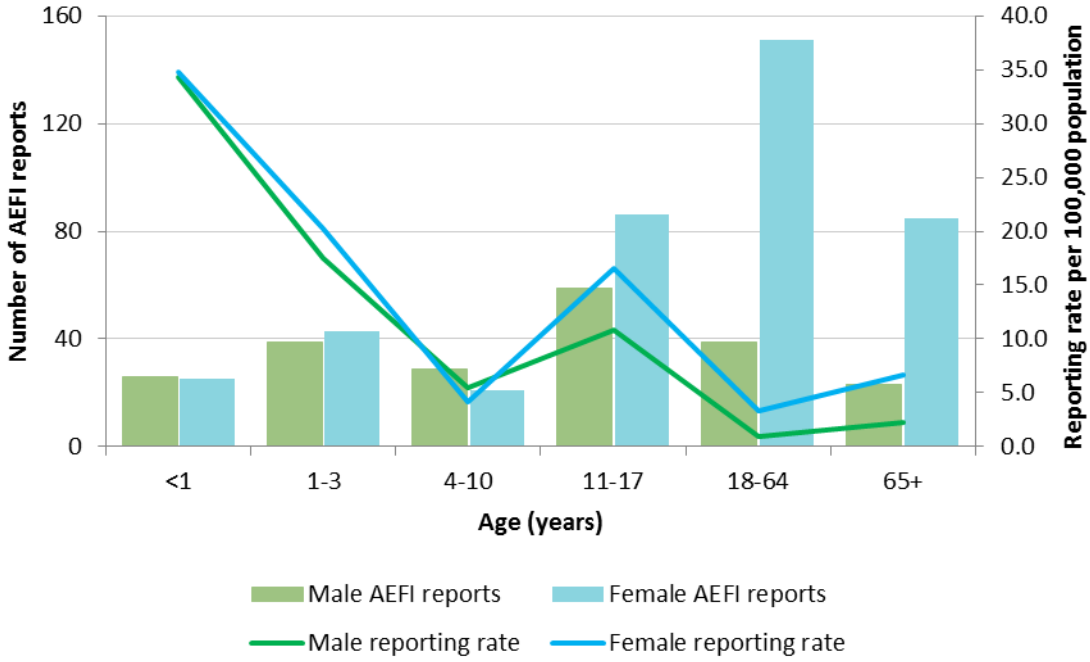
FIGURE 2. ANNUAL AEFI REPORTING RATE PER 100,000 POPULATION BY AGE GROUP: ONTARIO, 2012-16



AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2017/05/09].
Population: Population Projections [2016], Ontario Ministry of Health and Long-Term Care, IntelliHEALTH ONTARIO, extracted [2016/09/02].
Note: Excludes five reports with unknown age.

In 2016, the majority of all AEFI reports were in females (65.6%). Male predominance was observed only in the 4 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=3.7) followed by adults aged 65 years and older (RRR=3.0). The publicly funded HPV vaccination program included females only until September 2016 when the program was expanded to include boys (refer to Appendix 3 of Technical Annex). Therefore, a greater number of reports among females is expected in the 11 to 17 year age group for 2016 due to a higher number of doses of HPV vaccine administered to females in this age group.

FIGURE 3. NUMBER OF REPORTS AND REPORTING RATES OF AEFIS PER 100,000 POPULATION BY AGE GROUP AND SEX: ONTARIO, 2016

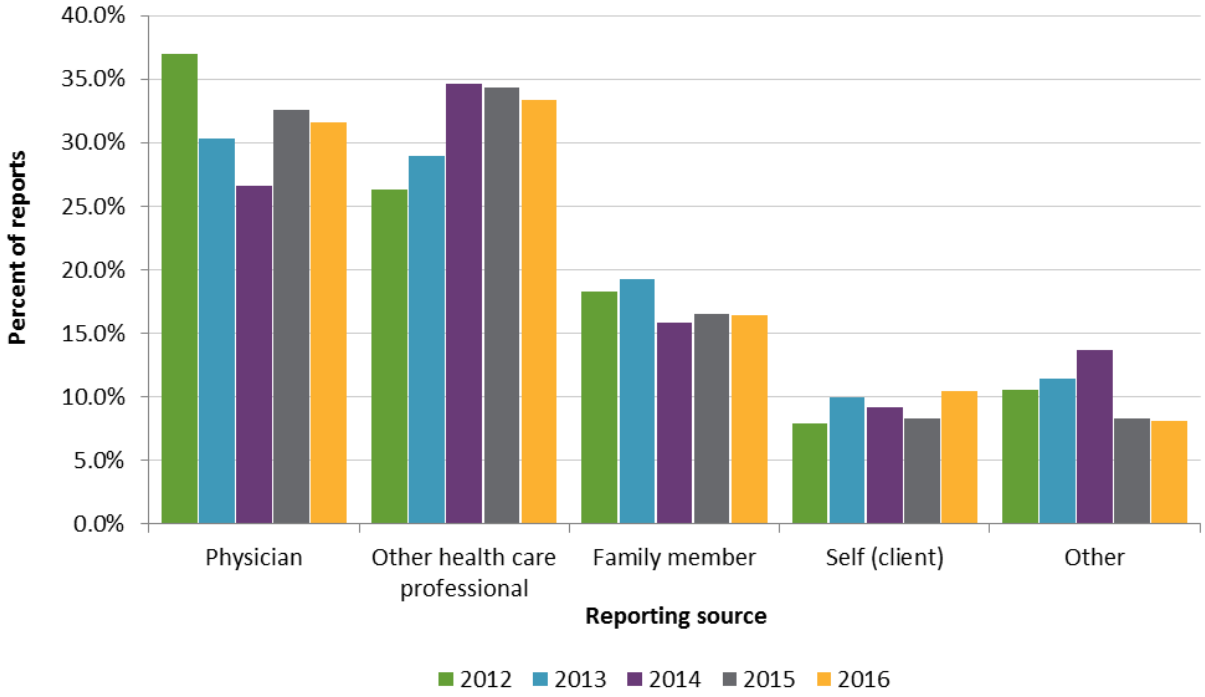


AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2017/05/09].
Population: Population Projections [2016], Ontario Ministry of Health and Long-Term Care, IntelliHEALTH ONTARIO, extracted [2016/09/02].
Note: Excludes two reports with unknown age (n=626).

Reporting source

In 2016, the majority of AEFIs were reported by physicians and other healthcare professionals (65.0%; 360 of 554 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 five-year period, whereas the proportion of reports from other healthcare professionals (e.g., nurses, pharmacists) has increased since 2012 and exceeded physician reports since 2014.

FIGURE 4. PERCENT DISTRIBUTION OF AEFIS BY REPORTING SOURCE: ONTARIO, 2012-16



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

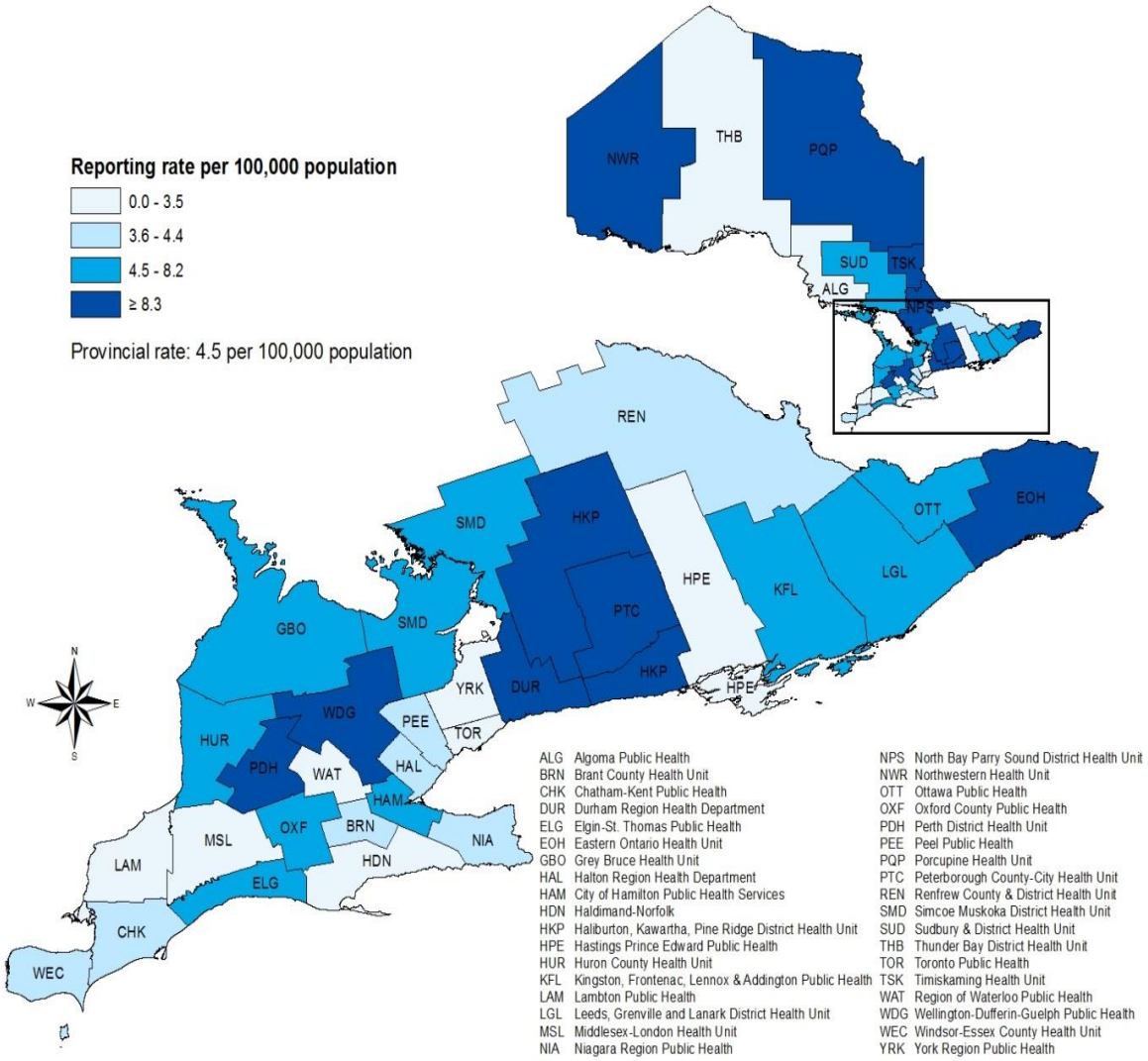
- Reporting source 'Other healthcare professional' includes the following iPHIS values: healthcare professionals, hospital, health area, lab, and branch office.
- Reporting source 'Other' includes the following iPHIS values: Facility, other agency, workplace, personnel, friend, detention centre and other (specify).
- Excludes 305 reports between 2012 and 2016 with unknown reporting source.

Geographic distribution

All vaccines

There was a wide variation in AEFI reporting by PHU in 2016 with PHU-specific reporting rates ranging from 0.0 to 30.8 per 100,000 population. Twenty PHUs (55.6%) met or exceeded the overall provincial AEFI reporting rate of 4.5 per 100,000 population in 2016, while the remainder (16 PHUs) were below the provincial rate, including the three most populated PHUs (Figure 5). Two PHUs did not report any AEFIs in 2016. There were six 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). See Appendix 1 for the total number of reports and reporting rates by PHU in 2016.

FIGURE 5. AEFI REPORTING RATE PER 100,000 POPULATION BY PUBLIC HEALTH UNIT: ONTARIO, 2016



AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2017/05/09].
Population: Population Projections [2016], Ontario Ministry of Health and Long-Term Care, IntelliHEALTH ONTARIO, extracted [2016/09/02].

Routine infant and early childhood vaccine series

The rate of AEFI reporting for children under four years of age also varied widely across the province. 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, or Var) the PHU-specific reporting rates ranged between 0.0 to 259.9 per 100,000 population (provincial rate of 19.8 per 100,000 population). There were 10 PHUs that reported zero AEFIs among this age group for any of these six vaccines (Figure 6).

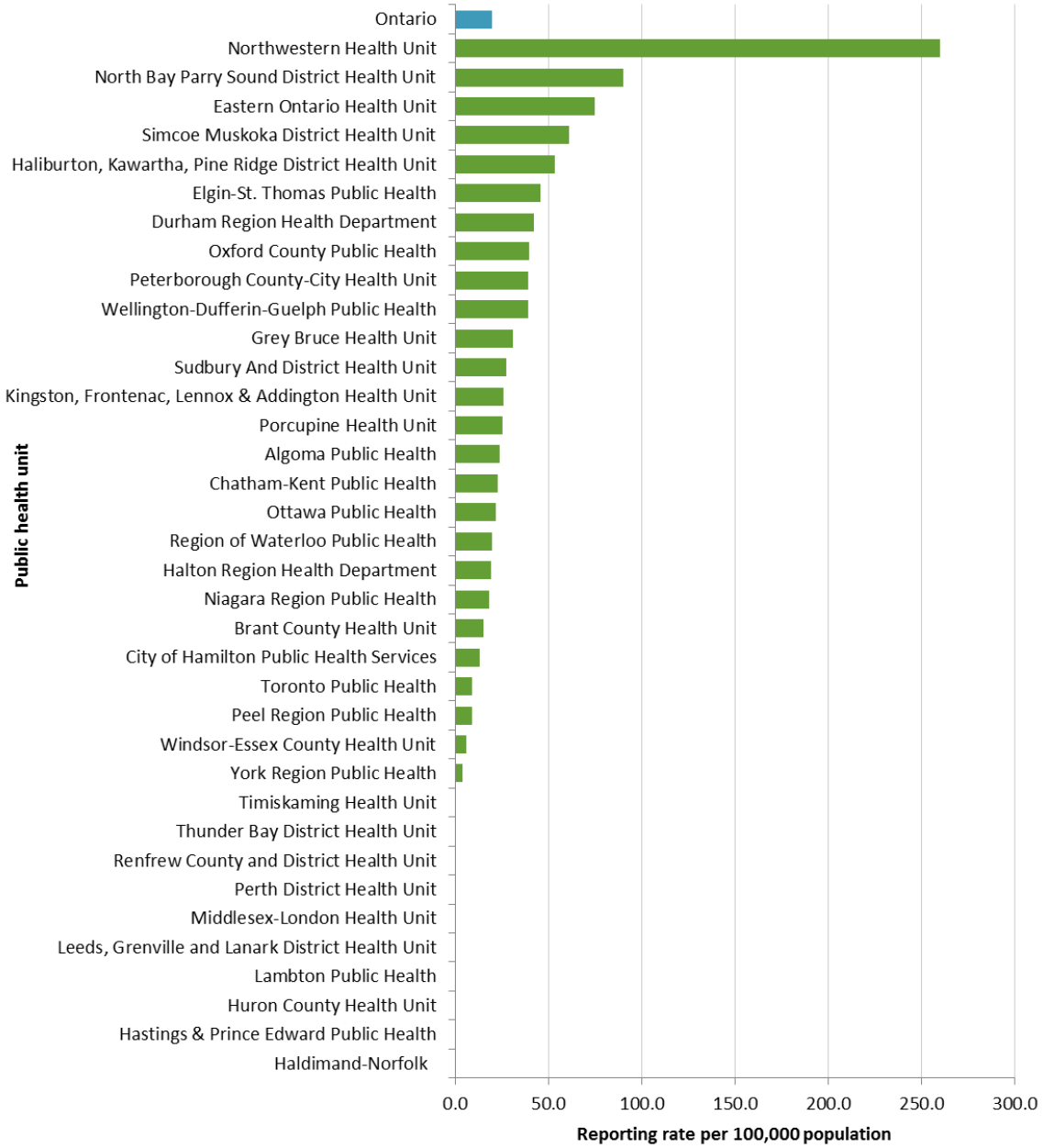
School-based vaccines

Geographic variation in reporting rates was also observed for AEFIs reported among 11- to 17-year-olds, following the three vaccines that are administered to adolescents by PHUs in school-based programs (Men-C-ACYW, HB and HPV4). The PHU-specific reporting rates ranged from 0.0 to 42.3 per 100,000 population, with a provincial rate of 10.8 per 100,000 population. Fifteen PHUs did not report any AEFIs for these three vaccines in 2016 (Figure 7).

Influenza vaccine

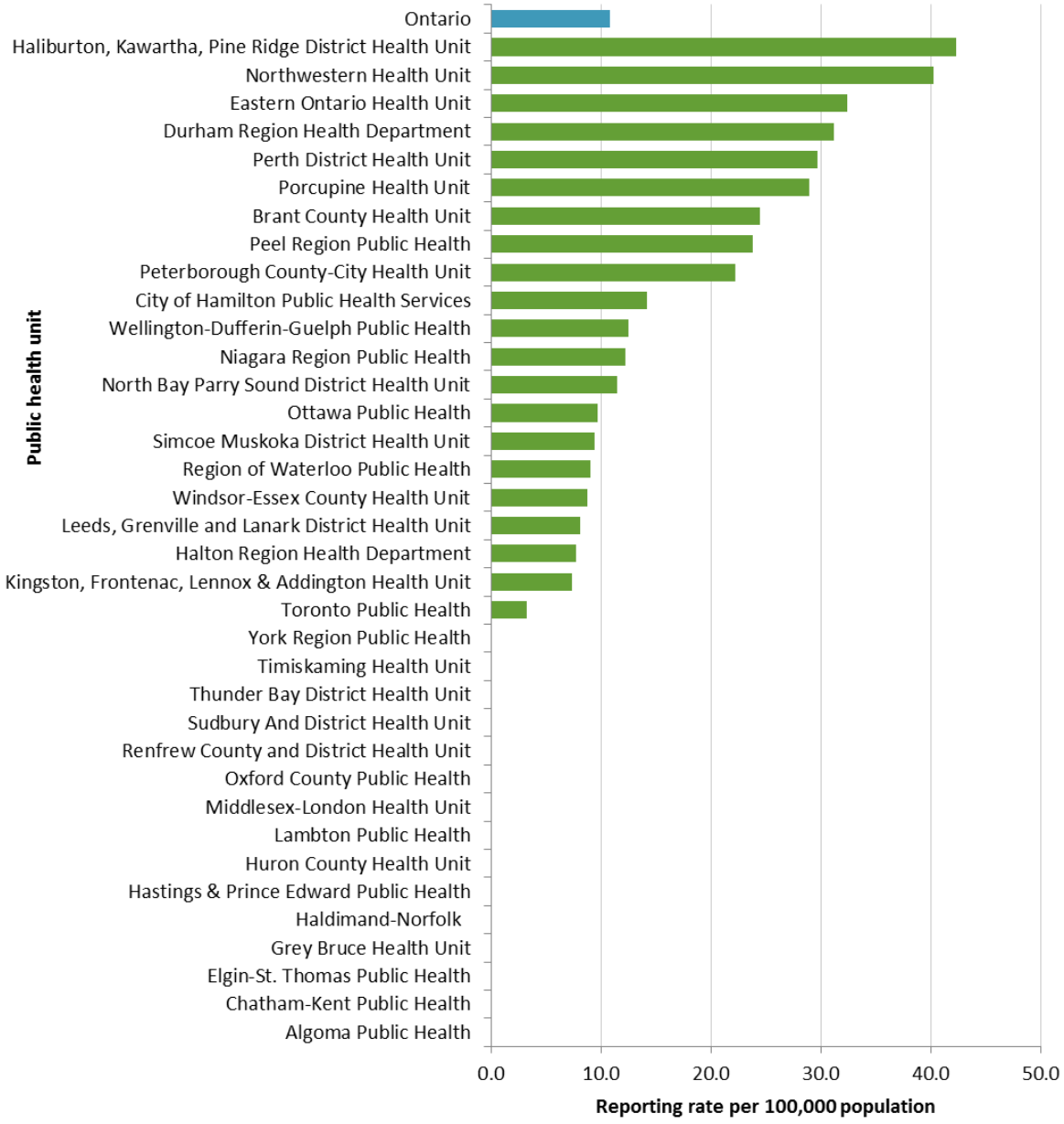
In 2016, 3,603,830 doses of influenza vaccine were distributed throughout the province, enabling calculation of influenza AEFI reports per 100,000 doses distributed in addition to per 100,000 population. Doses distributed are also available by PHU, and calculating reporting rates using doses distributed within each PHU as the denominator allows us to account for the variations in vaccine distribution between geographic areas. The overall PHU-specific reporting rates following influenza vaccine ranged from 0.0 to 19.2 per 100,000 doses distributed, with a provincial rate of 3.3 per 100,000 doses distributed. Ten of Ontario's 36 PHUs did not report any AEFIs following administration of influenza vaccine in 2016 (Figure 8).

FIGURE 6. REPORTING RATE PER 100,000 POPULATION FOR AEFIS AMONG CHILDREN UNDER FOUR YEARS OF AGE FOLLOWING DTAP-IPV-HIB, ROT-1, PNEU-C-13, MMR, MEN-C-C, OR VAR VACCINE BY PUBLIC HEALTH UNIT: ONTARIO, 2016



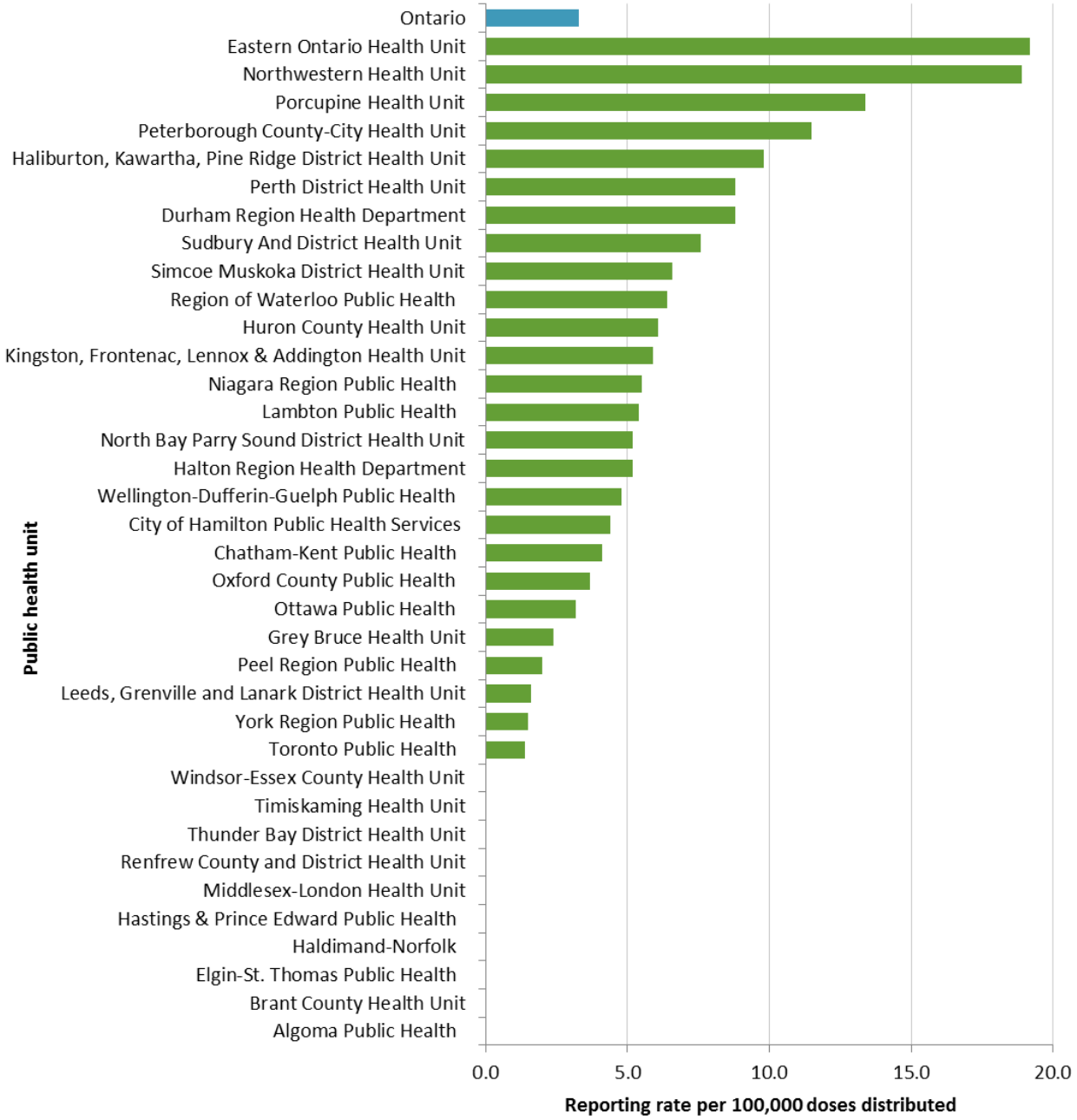
AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2017/05/09].
Population: Population Projections [2016], Ontario Ministry of Health and Long-Term Care, IntelliHEALTH ONTARIO, extracted [2016/09/02].
Note: Reporting rate includes AEFIs reported among children 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; 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, OR HPV4 VACCINE BY PUBLIC HEALTH UNIT: ONTARIO, 2016



AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2017/05/09].
Population: Population Projections [2016], Ontario Ministry of Health and Long-Term Care, IntelliHEALTH ONTARIO, extracted [2016/09/02].
Note: Reporting rate includes AEFIs reported among adolescents aged 11 to 17 years following administration of at least one of the following three vaccines: Men-C-ACYW, HB and HPV4. 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, 2016



AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2017/05/09].
Vaccine doses distributed: MOHLTC, Digital Health Immunization Repository, extracted by MOHLTC [2017/04/26].

Vaccines

In 2016, there were approximately 8 million doses of vaccines distributed in Ontario for the routine publicly funded immunization programs. Using doses distributed for each vaccine as the denominator, the highest vaccine-specific AEFI reporting rates in 2016 were observed for HPV4, Pneu-P-23, and HB vaccines (Table 1). Both HPV4 and HB vaccines are delivered through school-based programs and Pneu-P-23 is a vaccine routinely administered to persons 65 years and older. All three vaccines had low vaccine-specific serious reporting rates (<0.1 per 100,000 doses distributed). Although influenza vaccine was associated with the highest number of AEFI reports, it had the lowest AEFI reporting rate due to the high volume of doses distributed. The vaccine-specific serious reporting rates based on doses distributed were highest for DTaP-IPV-Hib and Pneu-C-13, both of which are administered to infants under one year of age; however, vaccine-specific serious reporting rates were low for all vaccines, ranging between 0.0 and 1.7 per 100,000 doses distributed. Refer to Serious AEFIs for further information.

For the trend in vaccine-specific reporting rates over time (2012 to 2016), see Appendix 2 or the Vaccine Safety Surveillance tool.

It is important to note that in September 2016, the school-based HPV program was expanded to include boys in grade seven and double cohort of girls (grades 7 and 8, for the 2016/17 school year). In addition, Zos was added to the publicly funded schedule for adults aged 65 to 70 years at the same time.

In order to look at trends over time in older adults, we examined population-based rates (as opposed to rates per doses distributed). Among adults aged 65 years and older, the age-specific reporting rate for Zos increased from 0.8 to 1.4 per 100,000 population between 2015 and 2016, while the reporting rate for Pneu-P-23 (a routine adult vaccine also administered as a one-dose series in this age group) stayed relatively consistent over this period (Figure 9).

TABLE 1. NUMBER OF REPORTS OF AEFIS AND AEFI REPORTING RATES PER 100,000 DOSES DISTRIBUTED BY VACCINE: ONTARIO, 2016

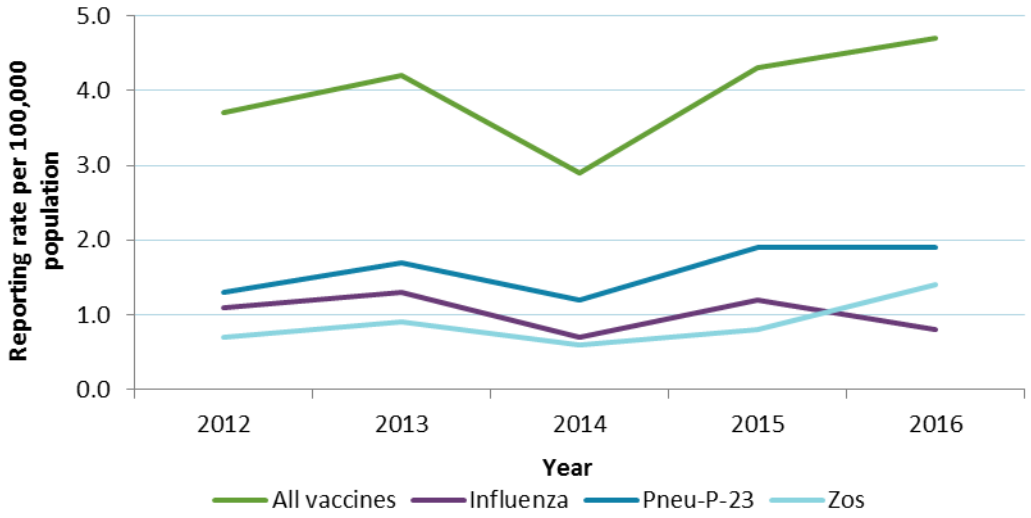
Vaccine[1]	Number of AEFI reports	Vaccine-specific reporting rate[2]	Number of serious reports	Vaccine-specific serious reporting rate[2]	Doses distributed[2]
Infant and childhood vaccines					
DTaP-IPV-Hib	67	11.7	10	1.7	574,321
Pneu-C-13	49	10.3	8	1.7	476,535
Rot-1	24	9.1	4	1.5	264,617
Men-C-C	21	10.1	2	1.0	207,992
MMR	37	13.5	2	0.7	274,688
Var	56	25.3	2	0.9	221,113
MMRV	18	10.4	0	0.0	173,828
Tdap-IPV	26	10.8	1	0.4	240,867
Adolescent vaccines					
Men-C-ACWY	38	20.8	2	1.1	182,604
HB	69	26.9	2	0.8	256,264
HPV4	69	32.9	1	0.5	209,474
Tdap	65	8.1	0	0.0	804,844
Routine adult vaccines					
Pneu-P-23	66	27.8	0	0.0	237,535
Td	7	3.4	0	0.0	203,574
Universal Influenza Immunization Program (UIIP)					
Inf	120	3.3	4	0.1	3,603,830
Other high-risk publicly funded, travel, and non-publicly funded 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]
HA	5	-	0	-	-
HAHB	8	-	0	-	-
HA-Typh-I	1	-	0	-	-
HPV-9	5	-	0	-	-
IPV	1	-	0	-	-
Men-B	10	-	1	-	-
Rab	6	-	0	-	-
Typh-I	1	-	0	-	-
YF	3	-	0	-	-
Zos[3]	53	-	1	-	-

AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2017/05/09].
Vaccine doses distributed: MOHLTC, Digital Health Immunization Repository, extracted by MOHLTC [2017/04/26].
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.[1]
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. Zos was added to the publicly funded schedule for individuals aged 65 to 70 years in September 2016. Zos will be grouped under 'Routine adult vaccines' starting in the 2017 report.

FIGURE 9. REPORTING RATE PER 100,000 POPULATION FOR AEFIS AMONG ADULTS AGED 65 YEARS AND OLDER FOLLOWING INF, PNEU-P-23, OR ZOS VACCINE: ONTARIO, 2012-16



AEFI reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2017/05/09].
Vaccine doses distributed: MOHLTC, Digital Health Immunization Repository, extracted by MOHLTC [2017/04/26].
Note: 'All vaccines' reporting rate includes AEFIs reported among adults aged 65 years and older following administration of at least one of the vaccines included in Table 1.

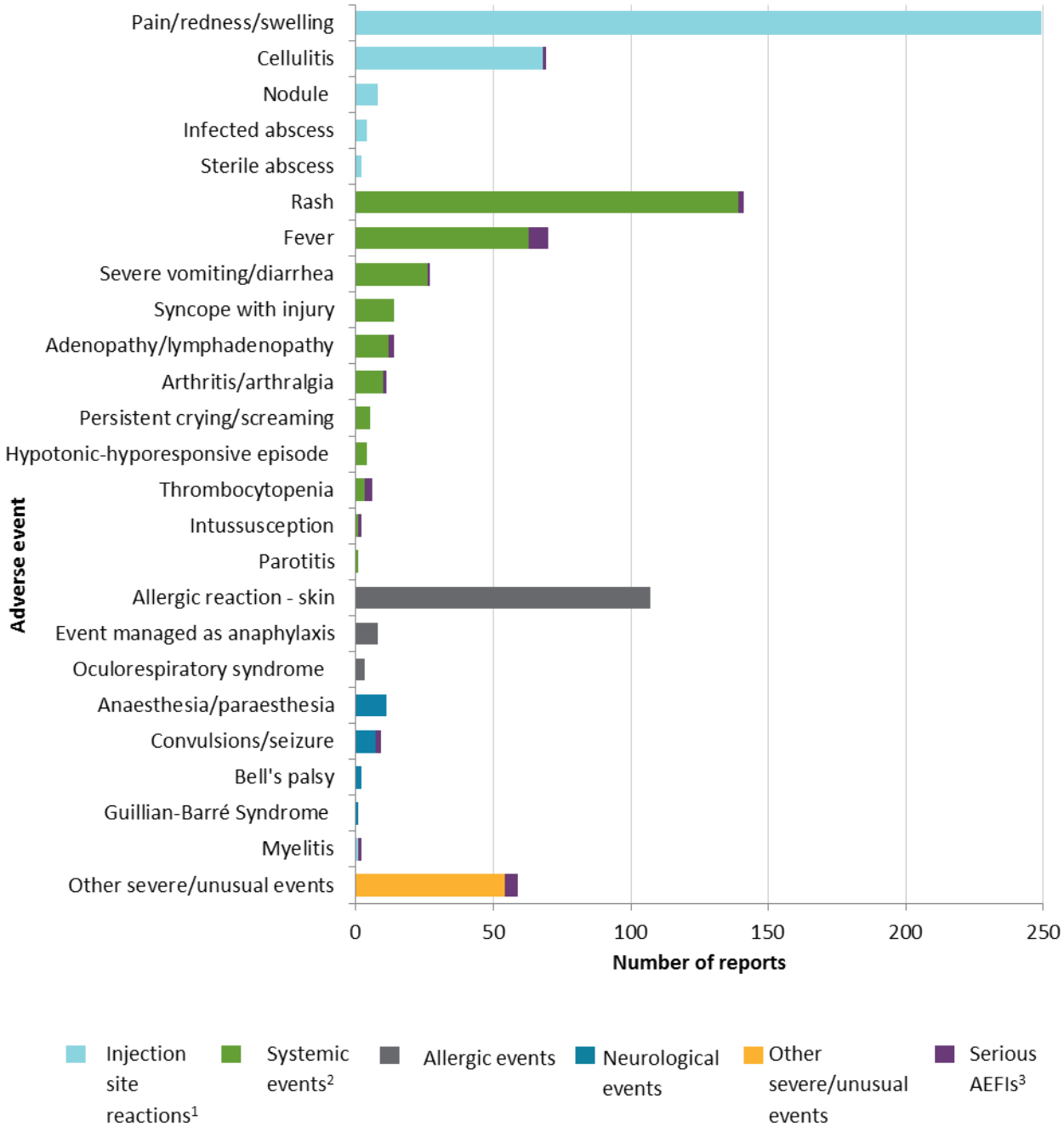
Adverse event descriptions

The type of adverse event was recorded in all reports (n=628) in 2016; 97.0% 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 10).

Injection site reactions were recorded in 48.7% of all reports (Table 2) and 99.7% of these were classified as non-serious. Injection site reaction was the only reported type of adverse event in 77.8% of these reports (n=238). Routinely administered vaccines that had the highest reporting rates for injection site reactions were Pneu-P-23 and Var (24.8 and 11.3 per 100,000 doses distributed, respectively).

The most frequently reported adverse event other than injection site reactions was rash, present in 22.1% of reports (n=139); 98.6% were classified as non-serious. Among those AEFI reports with rash, 41.0% (n=57) were associated with administration of a live virus vaccine (either MMR, MMRV, Var, or Zos) and 55.4% (n=31) of these occurred within 5 to 42 days of vaccine administration (i.e., within the expected range of time to rash onset for live virus vaccines). Among those, three rashes were confirmed as vaccine-strain by genotyping, including two that were measles vaccine strain (both following MMR vaccine, classified as non-serious), and one varicella-zoster vaccine strain (following Zoster vaccine) which was classified as serious (see further description in Serious AEFIs). For the trend in reporting of specific adverse events over time (2012 to 2016), see Appendix 2 or the Vaccine Safety Surveillance tool.

FIGURE 10. NUMBER OF NON-SERIOUS AND SERIOUS AEFI REPORTS BY ADVERSE EVENT AND CATEGORY: ONTARIO, 2016



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

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 AND CATEGORY: ONTARIO, 2016

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]	**306**	**48.7**	**1**
Cellulitis	68	10.8	1
Infected abscess	4	0.6	0
Nodule	8	1.3	0
Pain/redness/swelling at the injection site	249	39.6	0
Pain/redness/swelling extending beyond nearest joint	82	13.1	0
Pain/redness/swelling 4-10 days	158	25.2	0
Pain/redness/swelling >10 days	34	5.4	0
Sterile abscess	2	0.3	0
Systemic events[1]	**232**	**36.9**	**13**
Adenopathy/lymphadenopathy	12	1.9	2
Arthritis/arthralgia	10	1.6	1
Fever in conjunction with another reportable event	63	10.0	7
Hypotonic-hyporesponsive episode (HHE)	4	0.6	0
Intussusception[5]	1	0.2	1
Parotitis	1	0.2	0
Persistent crying/screaming	5	0.8	0
Rash	139	22.1	2
Severe vomiting/diarrhea	26	4.1	1
Syncope with injury	14	2.2	0
Thrombocytopenia[5]	3	0.5	3

Adverse event category[1]/ Adverse event[2]	Number of AEFI reports[3]	Percent of all AEFI reports (%)[4]	Number of serious AEFI reports
Allergic events[1]	**117**	**18.6**	**0**
Allergic reaction – skin	107	17.0	0
Event managed as anaphylaxis[5]	8	1.3	0
Oculorespiratory syndrome (ORS)	3	0.5	0
Neurologic events[1]	**21**	**3.3**	**3**
Anaesthesia/paraesthesia	11	1.8	0
Bell's palsy	2	0.3	0
Convulsions/seizures	7	1.1	2
Guillian-Barré syndrome[5]	1	0.2	0
Myelitis[5]	1	0.2	1
Other severe/unusual events	**54**	**8.6**	**5**

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. 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 2016.
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=628).
5. Classified as medically important events. See Technical Annex for further detail on the definition of medically important events.

There were 14 AEFIs reported that were classified as medically important events in 2016, representing 2.2% of all reports (please see the Technical Annex for a description of a medically important event). Five events also met the definition of a serious AEFI and are therefore described under Serious AEFIs, below. Of the remaining nine medically important events, there was one report of Guillian-Barré

syndrome in an adult after receiving one dose of Tdap and eight reports of events managed as anaphylaxis among persons who ranged in age from one to 72 years. Among the eight anaphylaxis reports, three were following HPV4 vaccine with one given concurrently with HB, two were associated with Inf and one each following DTaP-IPV-Hib, Var, and MMRV given with Tdap-IPV vaccine. The overall reporting rate of anaphylaxis within publicly funded vaccine programs was 1.0 per 1,000,000 doses distributed. All eight reports were assessed using the Brighton Collaboration standard definition of anaphylaxis.[2] Six met the Brighton definition, with four at level I of diagnostic certainty and two at level II. The remaining two reports did not have sufficient documented evidence to meet levels I, II or III of diagnostic certainty of the Brighton anaphylaxis case definition. None of the individuals reporting anaphylaxis were hospitalized and therefore, none were classified as serious.

Serious AEFIs

There were 19 AEFI reports in 2016 that were classified as serious, representing 3.0% (19/628) of all reports and a serious AEFI reporting rate of 1.4 per 1,000,000 population or 2.3 per 1,000,000 publicly funded doses distributed. All 19 serious AEFI reports were following administration of a publicly-funded vaccine. The majority of serious AEFIs (89.5%; n=17) occurred in individuals under 18 years of age, with most in children under four years (n=15). All serious AEFIs in 2016 were admitted to hospital for a mean length of stay of four days. There were eight serious AEFIs that were documented as being reported by IMPACT (Immunization Monitoring Program ACTive)[i], ranging from two months to three years of age. The proportion of AEFIs defined as serious remained relatively stable between 2012 and 2015 (range: 4.0% to 5.2%), but decreased to 3.0% in 2016. Based on case-level review, the most frequent type of adverse event reported among serious AEFIs in 2016 was febrile illness (63.2%; n=12, where 11 were in children under 10 years of age) including three diagnosed with Kawasaki disease (KD), two with seizure, two with rash (including one fatal case described below), and one each of thrombocytopenia, severe vomiting/diarrhea, lymphadenopathy, ischemic infarct, and arthritis/arthralgia. In addition, there were seven serious AEFIs without fever including two cases of thrombocytopenia and one each of intussusception, necrotizing enterocolitis, cellulitis, seizure, and myelitis. Of the 19 serious AEFIs in 2016, 21.1% (n=4) were documented to have been referred to the Special Immunization Clinic (SIC) Network[ii]; all were under one year of age. For more information about specific serious AEFI reports, please see Appendix 4.

There was one reported death in 2016 in an elderly adult on immune compromising medications who received Zos vaccine. The case developed disseminated zoster infection one month post vaccination. Disseminated varicella zoster infection caused by varicella zoster virus (VZV) vaccine-type virus (OKA strain) was confirmed post-mortem.

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[i] IMPACT is Canada's Immunization Monitoring Program ACTive, and is a paediatric hospital-based national active surveillance network for AEFI, 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.

[ii] Special Immunization Clinic (SIC) Network is established at 13 sites in Canada, and specializes in clinical assessment and vaccination of individuals with medically challenging AEFIs and other vaccine safety issues.

Healthcare utilization and outcome

Among those AEFI reports with healthcare utilization information completed in iPHIS, 71.5% (449/628) sought out-patient medical consultation, 25.8% (108/419) had an emergency room visit, and (3.0%; 19/628) were admitted to hospital.

In terms of AEFI outcomes, 91.2% (573/628) were either recovered at the time of assessment or were not yet recovered but likely to recover (69.1% and 22.1%, respectively). In a small proportion of reports (1.9%; n=12), 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 2016, 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 2016, 116 (18.5% of all AEFIs) reported an affirmative response to at least one of the three above risk factors. Of these, 83.6% (n=97) reported having a chronic illness/underlying medical condition, 9.5% (n=11) reported being immunocompromised and 6.9% (n=8) reported an immunization program error. Among immunization program errors, seven were related to administration errors (i.e., incorrect land-marking, expired vaccine, incorrect dose) and one was the result of non-adherence to vaccine indications or recommendations for use (i.e., 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

Overall, we found a low rate of AEFI reporting in Ontario following vaccines administered in 2016 and no unexpected vaccine safety issues.

The provincial AEFI reporting rate decreased in 2016 (4.5 per 100,000 population) as compared to 2015 (5.1 per 100,000 population). Decreases in the number of AEFI reports were observed for many vaccines that are routinely administered to children and adolescents, which typically drive the overall reporting rate due to the large volume of reports received in this group. This overall decrease in the provincial reporting rate was somewhat unexpected given that Ontario implemented two new publicly funded immunization programs (Zos for adults aged 65 to 70 years and HPV for boys in grade seven) later in 2016. An increase in reporting rate is typically expected with the implementation of new programs (the Weber effect);[3] however, because the two programs began in September 2016, it may be too early to detect changes in AEFI reporting.

As a comparison, the national AEFI reporting rate was 8.4 per 100,000 population in 2016,[4] and the Australian annual reporting rate was 13.2 per 100,000 population in 2014.[5] Although differences in population-based reporting rates are expected across different geographic areas due to variability in reporting requirements, case definitions, and population characteristics, Ontario's AEFI reporting rate has been consistently lower relative to other jurisdictions. The causes of Ontario's low reporting rate are likely multifactorial, but under-reporting of AEFIs likely plays an important role which has been highlighted in previous reports.[6-8] The data in 2016 suggests that health care professionals (HCPs) are under-reporting AEFIs as out of 449 AEFI reports where medical consultation was sought, only 277 (61.7%) were recorded as being reported by a physician or other HCP. Although the reasons for under-reporting of AEFIs, particularly by HCPs, are not yet fully understood in Ontario, surveys from other jurisdictions have identified a number of barriers to reporting including lack of familiarity with the AEFI reporting process, uncertainty with who is responsible for reporting, unclear definitions of a reportable AEFI, and the amount of time required to complete a report.[9-11] Since July 2016, as a strategy to improve health care provider awareness of AEFI reporting requirements, PHUs have been required by the MOHLTC to share PHO's AEFI reporting factsheet during their routine annual cold-chain inspections. While it is too early to assess the impact of this initiative, the lower reporting rate in 2016 suggests that there has not been any impact thus far.

In 2016, there was a wide variation in population-based AEFI reporting by PHUs for both infant and early childhood vaccine programs, and school-based programs. This high geographic variability in AEFI reporting rates may be an indicator of variability in interpretation and reporting processes of AEFIs across the province which then drives the provincial AEFI reporting. There were six PHUs that did not report AEFIs in any of three categories which comprise the majority of vaccine doses distributed for the publicly funded program in the province (routine infant and early childhood vaccines, school-based

vaccines and influenza vaccine). It is important to note that population-based reporting rates have limitations as they assume similar distribution and/or uptake of vaccines per population. In order to explore this further, we examined both population-based and dose-based reporting rates by PHU for influenza vaccine (data not shown; population-based rates available in the Vaccine Safety Surveillance tool). The geographic variability in reporting persisted in both types of reporting rates, but the ranking of PHUs by reporting rate differed between population-based and dose-based rates, showing that population-based reporting rates are not a perfect proxy for AEFI reporting rates based on doses distributed. Although doses distributed enables a more accurate comparison of AEFI reporting rates across geographic areas by taking into account the differences in vaccine distribution, a population-based provincial immunization registry would be most accurate, allowing assessment of the number of doses administered to individuals residing in each area and enabling the estimation of the true incidence of AEFI reporting by vaccine or event type.

As with previous years, the 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.[1] Of note, compared to 2015, the reporting rate for infants under one year of age increased in 2016 and surpassed that of children aged 1 to 3 years, similar to trends observed in 2012 and 2013. The increase in AEFIs in infants may be due to increases in reports following DTaP-IPV-Hib and Rot-1 in 2016 (28.8% and 26.3% increase compared to 2015, respectively), which are typically given to infants under one year. The rates in infants may also have surpassed the 1 to 3 year olds due to decreases in the number of AEFI reports following Men-C-C and MMR in 2016 (46.2% and 50.0% decrease compared to 2015, respectively), which are typically administered within the 1 to 3 year old age group. A female predominance in AEFI reports, particularly among adults, is consistently observed in Ontario[12] as well as in other passive AEFI surveillance systems.[13,14] Among adolescents 11-to 17-years old, we expect that the female predominance observed between the years 2012 and 2016 will be reduced going forward, due to the expansion of the publicly funded HPV vaccination program to grade seven males in September 2016.

Vaccine-specific reporting rates in 2016 were highest for HPV4 and HB, two vaccines primarily delivered by PHUs within school-based programs where we tend to have higher AEFI reporting overall, and 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.[15] Of note, both the number of reported AEFIs and doses distributed increased for HPV4, resulting in a slightly increased reporting rate in 2016 compared to 2015 (29.5 to 32.9 per 100,000 doses distributed), likely reflecting the expansion of the HPV4 vaccination program. In addition, the reporting rate for Zos among those over 65 years of age increased between 2015 and 2016, whereas the reporting of Pneu-P-23 stayed relatively stable for the same age group. This trend likely reflects the introduction of Zos vaccine into the publicly funded immunization schedule for adults over 65 years of age. With the addition of males to the HPV4 program, we expect to see an initial increase followed by stabilization of the AEFI reporting rate, which is often expected with the addition of new vaccines or populations to routine programs.[3]

Among all publicly funded vaccines, influenza had the highest volume of vaccine distribution at approximately 3.6 million doses but has a low reporting rate of 3.3 per 100,000 doses distributed.

Although the number of doses distributed for influenza decreased by approximately a million doses in 2016 compared to 2015, this low reporting rate relative to high volume of vaccine distribution has also been observed in other passive AEFI surveillance systems.[14,16] Similar to previous years, under-reporting is one possible factor which may affect the influenza AEFI reporting rate as influenza vaccine is administered by HCPs in a wide variety of community-based and institutional settings that do not necessarily provide other routine immunizations. Thus, these immunization providers may have varying levels of familiarity with reporting requirements and do not necessarily have an ongoing primary health care relationship with vaccine recipients, making them less likely to be aware or consulted if an adverse event occurs.

The types of AEFIs reported in 2016 were similar to previous years in which mild events (e.g., injection site reactions and 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.[13,14] 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 2.2 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. Slightly less than half (41.0%) of rash reports were associated with live virus vaccines which are known to produce virus-like rashes, particularly after the first dose (up to 5%-10% and 3%-5% for MMR and varicella vaccines, respectively).[17,18]

Serious AEFIs were very rarely reported in 2016, and the rate of serious AEFIs was also at its lowest in the past five years. This decrease is consistent with the decrease in the overall AEFI reporting rate this year. The decrease in reports of serious AEFIs could also be due to factors such as under-reporting and inaccurate data entry of fields (e.g., hospitalization) in iPHIS that are required to identify serious AEFIs. Efforts are underway to reconcile all AEFI reports entered in iPHIS against external sources, such as the database from PHAC and/or IMPACT, to help confirm the completeness of serious reports identified in iPHIS. The types of serious AEFIs reported were most often related to events known to be rarely reported following immunization. For example, Kawasaki disease (KD) is a rare condition of unknown etiology that primarily affects young children. While the evidence of a causal association between immunization and KD is lacking, it has been observed in temporal relation to immunization.[19] Given the unknown etiology of KD, a small number of reports of KD are expected every year following immunization in young children.

There was one report of a death among the serious AEFIs reported in 2016. The death was following receipt of Zos (Zostavax®) vaccine in an elderly individual on immune compromising medications. In general, live vaccines, including Zos, are contraindicated in immunocompromised persons and persons on immune compromising medications because there is a risk of illness caused by the weakened vaccine strain of the virus.[20]

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 2016 as well as reporting trends since 2012. 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 had recovered at the time of reporting. Ongoing surveillance of AEFIs in Ontario is needed to monitor vaccine safety and to further understand and develop strategies to address under-reporting within the surveillance system.

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Appendices

Appendix 1: Number of AEFI reports and reporting rates of AEFIs per 100,000 population by public health unit, 2016

Public health unit	Number of AEFI reports	Population	Reporting rate per 100,000 population
Ontario	**628**	**13,959,900**	**4.5**
Northwestern Health Unit	25	81,290	30.8
Eastern Ontario Health Unit	39	205,343	19.0
Porcupine Health Unit	11	85,925	12.8
Peterborough County-City Health Unit	17	140,562	12.1
Haliburton, Kawartha, Pine Ridge District Health Unit	20	181,270	11.0
North Bay Parry Sound District Health Unit	14	127,986	10.9
Durham Region Health Department	70	669,724	10.5
Perth District Health Unit	7	78,538	8.9
Timiskaming Health Unit	3	33,913	8.8
Wellington-Dufferin-Guelph Public Health	24	288,287	8.3
Elgin-St. Thomas Public Health	6	90,963	6.6
Simcoe Muskoka District Health Unit	37	556,618	6.6
Oxford County Public Health	7	112,814	6.2
Grey Bruce Health Unit	10	163,780	6.1
Sudbury And District Health Unit	12	198,308	6.1
Ottawa Public Health	53	971,723	5.5

Public health unit	Number of AEFI reports	Population	Reporting rate per 100,000 population
Kingston, Frontenac, Lennox & Addington Health Unit	11	203,800	5.4
Huron County Health Unit	3	58,270	5.1
City of Hamilton Public Health Services	28	562,534	5.0
Leeds, Grenville and Lanark District Health Unit	8	169,543	4.7
Halton Region Health Department	25	570,427	4.4
Niagara Region Public Health	20	451,702	4.4
Brant County Health Unit	6	146,751	4.1
Chatham-Kent Public Health	4	105,592	3.8
Renfrew County and District Health Unit	4	106,184	3.8
Windsor-Essex County Health Unit	15	405,247	3.7
Peel Region Public Health	53	146,6743	3.6
Region of Waterloo Public Health	16	548,526	2.9
Algoma Public Health	3	114,548	2.6
Hastings & Prince Edward Public Health	4	163,666	2.4
Toronto Public Health	59	2,870,396	2.1
Lambton Public Health	2	129,389	1.5
York Region Public Health	10	1,159,873	0.9
Middlesex-London Health Unit	2	474,453	0.4
Haldimand-Norfolk	0	110,594	0.0
Thunder Bay District Health Unit	0	154,618	0.0

AEFI Reports: MOHLTC, integrated Public Health Information System (iPHIS) database, extracted [2017/05/09].
Population: Population Projections [2016], Ontario Ministry of Health and Long-Term Care, IntelliHEALTH ONTARIO, extracted [2016/09/02].

Appendix 2: Number of AEFI reports and reporting rates of AEFIs per 100,000 doses distributed by vaccine, 2012-16

Vaccine[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016
	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	73	12.9	55	9.7	52	9.1	67	11.7
Pneu-C-13	49	11.0	56	12.8	54	12.5	59	12.6	49	10.3
Rot-1	24	9.8	26	9.9	21	8.1	19	7.1	24	9.1
Men-C-C	15	9.7	22	14.8	26	16.2	39	19.5	21	10.1
MMR	37	12.8	48	15.9	50	18.4	74	21.6	37	13.5
Var	59	15.9	61	20.1	54	20.5	57	21.8	56	25.3
MMRV	4	14.1	4	14.1	1	1.0	16	10.0	18	10.4
DTaP-IPV	54	105.9	8	340.4	13	N/A	1	18.0	0	0.0
Tdap-IPV	13	9.0	27	13.0	8	3.8	30	12.3	26	10.8
Adolescent vaccines										
Men-C-ACWY	25	21.2	43	36.0	42	25.9	60	36.5	38	20.8

Vaccine[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016
	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]
HB	58	24.5	67	25.0	47	17.5	56	22.2	69	26.9
HPV4	47	27.3	48	27.0	39	24.4	42	29.5	69	32.9
Tdap	61	9.2	56	8.3	75	11.9	84	10.6	65	8.1
Routine adult vaccines										
Pneu-P-23	42	20.6	59	25.1	35	14.5	63	23.1	66	27.8
Td	11	3.5	13	4.7	6	2.2	6	2.4	7	3.4
Td-IPV	1	4.1	0	0.0	0	0.0	1	5.1	0	0.0
Universal Influenza Immunization Program (UIIP)										
Inf	199	5.3	189	4.5	153	3.4	165	3.6	120	3.3
Other high-risk publicly funded, travel, and non-publicly funded vaccines										
BCG	1	-	0	-	0	-	0	-	0	-
Chol-Ecol-O	1	-	1	-	1	-	1	-	0	-
Chol-O	0	-	1	-	0	-	0	-	0	-
HA	2	-	3	-	3	-	5	-	5	-
HAHB	10	-	7	-	17	-	15	-	8	-

Vaccine[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016
	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]
HA-Typh-I	3	-	5	-	0	-	1	-	1	-
Hib	0	-	3	-	0	-	0	-	0	-
HPV2	1	-	1	-	0	-	0	-	0	-
HPV9	0	-	0	-	0	-	4	-	5	-
IPV	3	-	0	-	1	-	1	-	1	-
JE	1	-	0	-	0	-	0	-	0	-
Men-B	0	-	0	-	3	-	3	-	10	-
Rab	5	-	8	-	6	-	2	-	6	-
Typh-I	6	-	1	-	3	-	2	-	1	-
Typh-O	2	-	1	-	1	-	0	-	0	-
YF	8	-	7	-	5	-	4	-	3	-
Zos[3]	31	-	42	-	40	-	59	-	53	-
Total AEFIs[4]	**682**		**694**		**599**		**710**		**628**	

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

Vaccine doses distributed: MOHLTC, Digital Health Immunization Repository, extracted by MOHLTC [2017/04/26].

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. 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. Zos was added to the publicly funded program in September 2016.
4. 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 and category, 2012-16

Adverse event category[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016
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]**
Injection site reactions[1]	**277**	**40.6**	**282**	**40.8**	**263**	**44.1**	**303**	**43.0**	**306**	**48.7**
Cellulitis	61	8.9	63	9.1	47	7.9	72	10.5	68	10.8
Infected abscess	4	0.6	6	0.9	2	0.3	1	0.1	4	0.6
Nodule	23	3.4	11	1.6	14	2.3	7	1.0	8	1.3
Pain/redness/swelling at the injection site	209	30.6	233	33.7	215	36.0	244	34.2	249	39.6
Pain/redness/swelling extending beyond nearest joint	17	2.5	58	8.4	70	11.7	57	8.4	82	13.1
Pain/redness/swelling <4 days[3]	61	8.9	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Pain/redness/swelling ≥4 days[3]	63	9.2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Pain/redness/swelling 4-10 days[4]	61	8.9	156	22.5	130	21.8	160	22.2	158	25.2
Pain/redness/swelling >10 days[4]	22	3.2	39	5.6	36	6.0	50	7.0	34	5.4
Sterile abscess	7	1.0	0	0.0	5	0.8	1	0.1	2	0.3
Systemic events[1]	**203**	**29.8**	**259**	**37.4**	**221**	**37.0**	**292**	**41.2**	**232**	**36.9**

Adverse event category[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016
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]**
Adenopathy/ lymphadenopathy	5	0.7	10	1.4	8	1.3	10	1.4	12	1.9
Arthritis/arthralgia	11	1.6	14	2.0	15	2.5	16	2.3	10	1.6
Fever in conjunction with another reportable event	55	8.1	62	9.0	72	12.1	91	12.9	63	10.0
Hypotonic-hyporesponsive episode (HHE)	5	0.7	3	0.4	7	1.2	3	0.4	4	0.6
Intussusception[5]	0	0.0	1	0.1	0	0.0	4	0.6	1	0.2
Parotitis	2	0.3	1	0.1	0	0.0	2	0.3	1	0.2
Persistent crying/screaming	6	0.9	6	0.9	7	1.2	3	0.4	5	0.8
Rash	147	21.6	157	22.7	130	21.8	177	25.0	139	22.1
Severe vomiting/diarrhea[4]	6	0.9	35	5.1	27	4.5	34	4.8	26	4.1
Syncope with injury[4]	0	0.0	6	0.9	11	1.8	18	2.5	14	2.2
Thrombocytopenia[5]	0	0.0	2	0.3	0	0.0	1	0.1	3	0.5
Allergic events[1]	**170**	**24.9**	**143**	**20.7**	**115**	**19.3**	**142**	**20.1**	**117**	**18.6**
Allergic reaction – other[3]	16	2.3	0	0.0	0	0.0	0	0.0	0	0.0
Allergic reaction – skin	134	19.6	130	18.8	96	16.1	124	17.5	107	17.0

Adverse event category[1]	2012	2012	2013	2013	2014	2014	2015	2015	2016	2016
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]**
Event managed as anaphylaxis[5]	20	2.9	17	2.5	12	2.0	16	2.3	8	1.3
Oculorespiratory syndrome (ORS)	6	0.9	1	0.1	7	1.2	6	0.8	3	0.5
Neurologic events[1]	**31**	**4.5**	**36**	**5.2**	**24**	**4.0**	**40**	**5.6**	**21**	**3.3**
Acute disseminated encephalomyelitis (ADEM)[5]	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
Anaesthesia/paraesthesia[4]	7	1.0	15	2.2	7	1.2	18	2.5	11	1.8
Bell's palsy	3	0.4	2	0.3	2	0.3	6	0.8	2	0.3
Convulsions/seizures	14	2.1	14	2.0	11	1.8	12	1.7	7	1.1
Encephalopathy/encephalitis[5]	2	0.3	1	0.1	0	0.0	0	0.0	0	0.0
Guillian-Barré syndrome[5]	2	0.3	2	0.3	1	0.2	3	0.4	1	0.2
Meningitis[5]	0	0.0	1	0.1	2	0.3	2	0.3	0	0.0
Myelitis[5]	0	0.0	0	0.0	0	0.0	2	0.3	1	0.2
Paralysis other than Bell's palsy	3	0.4	1	0.1	2	0.3	0	0.0	0	0.0
Other severe/ unusual events[1]	**141**	**20.7**	**100**	**14.5**	**85**	**14.2**	**81**	**11.4**	**54**	**8.6**
Total AEFIs[6]	**682**		**692**		**597**		**708**		**628**	

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, 2016

Event-type[1]	Number of AEFI reports	Age group (years)	Associated vaccines[2]	Additional information
Febrile illness	12	<1 (n=6) 1-3 (n=4) 4-10 (n=1) 65+ (n=1)	DTaP-IPV-Hib, HB, Inf, Men-C-ACWY, Men-B, Men-C-C, MMR, Pneu-C-13, Rot-1, Tdap-IPV, Var, Zos	Three with Kawasaki disease, two with seizure, two with rash*, one each of severe vomiting/diarrhea, lymphadenopathy, ischemic infarct, thrombocytopenia, and arthritis/arthralgia. *The rash following Zos in a 65+ year old individual was a fatal case.
Thrombocytopenia	2	<1 (n=1) 11-17 (n=1)	DTaP-IPV-Hib, HB, HPV4, Inf, Men-C-ACWY, Pneu-C-13, Rot-1	-
Cellulitis	1	<1	DTaP-IPV-Hib, Pneu-C-13	-
Intussusception	1	<1	DTaP-IPV-Hib, Pneu-C-13, Rot-1	-
Myelitis	1	18-64	Inf	Onset of bilateral leg weakness and paresthesia six days after receiving vaccine.
Necrotizing enterocolitis	1	<1	DTaP-IPV-Hib, Pneu-C-13, Rot-1	Onset within 1.5 hours after receiving vaccines.
Seizure	1	<1	DTaP-IPV-Hib	-

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

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)”.
2. Includes vaccines that were co-administered.

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

647.260.7100
communications@oahpp.ca
publichealthontario.ca