Appendix 1: Summary of rates of anaphylaxis following immunization (by surveillance system type and vaccine)

Author	Year	Country	Target population	AEFI assessment	Anaphylaxis definition	Vaccine	No. of events	Doses	Administered or distributed?	Anaphylaxis rate per 100 000	95% Poisson CI
School-based programs											
New South Wales	Apr–Dec 2007	New South Wales, Australia	15–18 years	• School-based and routine provider-based passive surveillance	• Brighton classification[1]	Quadrivalent HPV	7	269 680	Administered	2.6	1.0–5.3
D'Souza et al.[2]	Aug–Nov 1998	Australia	Males and females 5–12 years	• School-based and routine provider-based passive surveillance	• Anaphylactoid: exaggerated allergic reaction occurring within 2 hours of immunization characterized by 1 or more of wheezing and shortness of breath due to bronchospasm; laryngospasm/laryngeal edema; or skin manifestations • Anaphylaxis: circulatory failure occurring within minutes of immunization with or without bronchospasm and/or laryngospasm/laryngeal edema	MMR	7	1 700 000	Administered	0.4	0.2–0.8
NSW Department of Health, unpublished data	2003	New South Wales, Australia	Males and females 5–19 years	• School-based and routine provider-based passive surveillance	• As per *The Australian Immunisation Handbook*[3]	Conjugated meningococcal C	1	823 197	Administered	0.1	0.003–0.68
Dobson et al.[4]	1992	British Columbia, Canada	Males and females 10–12 years	• School-based passive surveillance plus active surveillance of pediatricians using mailed cards after each dose and telephone contact	• Not given	Hepatitis B	1	127 922	Administered	0.8	0.02–4.36
UK Department of Health[5]	1994	United Kingdom	Routine childhood vaccination plus targeted campaign 7.17 million children 5–16 years	• School-based and routine provider-based passive surveillance • High priority handling of MR vaccines reports • Daily electronic transfer to program database • Active seeking of follow-up if "Yellow Card" info inadequate	• Not given • 123 reports of immediate allergic type reactions allergy or anaphylaxis within 24 hours (1. 5 per 100 000)	Measles–rubella	80*	8 000 000	Administered	1.0	0.8–1.2

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Appendix to: Brotherton JML, Gold MS, Kemp AS, et al. Anaphylaxis following quadrivalent human papillomavirus vaccination. *CMAJ* 2008;179:525-33.

Enhanced surveillance systems											
Sakaguchi et al.[6]	Apr 1994–Mar 1997	Japan	Measles: males and females aged 1 year. Other vaccines during infancy after measles.	• Physicians and vaccine manufacturers submitted clinical data and serum samples from children with systemic immediate hypersensitivity reactions to live virus vaccines containing gelatin • Submitted in order to access anti-gelatin IgE testing	• Within 1 hour of vaccination • Severe: cutaneous signs plus airway obstruction or anaphylactic shock • Mild: cutaneous signs plus respiratory symptoms (wheezing and/or cough or laryngeal edema) without airway obstruction	Measles	59	3 507 090	Distributed	1.7	1.3–2.2
						Mumps	9	458 828	Distributed	2.0	0.9–3.7
						Rubella	24	1 503 838	Distributed	1.6	1.0–2.4
						Varicella	16	679 513	Distributed	2.4	1.3–3.8
						Varicella 1996 (peak rate)	12	265 594	Distributed	4.5	2.3–7.9
Patja et al.[7,8]	1982–1996	Finland	Males and females 14 months and 6 years, plus catch-up initially. In 1988, 11–13 year old girls, health care workers, nursing students. New mothers 1988–1993. Defence personnel 1986. 1.8 million individuals vaccinated.	• Passive surveillance through health care providers • Prospective follow-up of notified serious adverse events	• Not defined • Of 30 suspected cases notified, in 15 cases the physician ultimately diagnosed fainting	MMR	15	2 990 000	Administered	0.05	0.028–0.082
Bohlke et al.[9]	1991–1997	United States	2 226 907 males and females aged 0–17 years enrolled in 1 of 4 US Health Maintenance Organizations	• Vaccine Safety Datalink Project • Automated linkage of immunization records with medical records from hospitalizations, emergency department visits and some outpatient visits containing ICD-9 codes suggestive of anaphylaxis • Reviewed diagnoses of interest for 657/664 identified as occurring within 0–2 days of vaccination including chart review of other possible ICD-9 codes of interest (allergy related) at 1 site	• Probable anaphylaxis: manifestations involving >1 organ system (cutaneous, respiratory, cardiovascular, gastrointestinal) occurring within 4 hours of exposure to precipitant with subsequent treatment • Possible anaphylaxis: (1) as for probable but untreated; or (2) involvement of >1 organ system occurring after 4 hours or indeterminate time period, treated; or (3) only 1 system involved, symptoms within 4 hours, treated	All vaccines, all study sites	5	7 644 049	Administered	0.1	0.021–0.153
						All vaccines, enhanced site	1	653 990	Administered	0.2	0.004–0.852

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Passive national surveillance systems											
Nakayama and Onoda[10]	1994–2004	Japan	Male and female population	• Passive national surveillance from physicians	• Urticaria or angioedema with respiratory symptoms, cardiovascular shock or both	Japanese encephalitis	6	9 450 000	Distributed	0.1	0.02–0.14
						DTPa	10	10 560 000	Distributed	0.1	0.05–0.17
						Influenza	26	38 020 000	Distributed	0.1	0.04–0.10
Pool et al.[11]	1991–1997	United States	Male and female population	• VAERS – passive national surveillance • Reports from any source	• Probable anaphylaxis: evidence of a mast-cell mediated reaction including at least 1 dermatological sign or symptom and 1 or more specified signs and symptoms from respiratory, cardiovascular or gastrointestinal systems within 4 hours • Possible anaphylaxis: respiratory or dermatologic symptoms but not both within 4 hours of immunization OR 1 or both respiratory and dermatological symptoms but > 4 hours post immunization	MMR	168	94 000 000	Distributed	0.2	0.15–0.21
UK Department of Health[12]	1997–2003	United Kingdom	Male and female population	• Passive surveillance "Yellow Cards"	• As per the Green Book[12]	All vaccines	130	117 000 000	Distributed	0.1	0.09–0.13
Zhou et al.[13]	1991–2001	United States	Male and female population	• VAERS – passive national surveillance • Reports from any source	• As per VAERS classification system (COSTART) "anaphylactoid"	All vaccines	452	1 900 000 000	Distributed	0.02	0.022–0.026
Kelso et al.[14]	1990–1997	United States	Male and female population	• VAERS – passive national surveillance • Reports from any source	• All yellow fever reports reviewed (n=243), 40 possible or probable anaphylaxis • Probable: within 4 hours of vaccination and with both dermatological and respiratory signs/symptoms • Possible: either dermatological or respiratory symptoms within 4 hours or both occurring later than 4 hours	Yellow fever	40	5 236 820	Distributed	0.8	0.5–1.0

Note: AEFI = adverse events following immunization, DTPa = diphtheria–tetanus–pertussis (acellular), MMR = measles–mumps–rubella, VAERS = Vaccine Adverse Event Reporting System.
* Not given in the publication. We calculated this from published denominator and anaphylaxis rate.

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