Supplement: Full Tables by Condition, References, and Incidence Rates

Abbreviations

y=Year(s); m=Month(s); w=Week(s); d=Day(s); h=Hour(s)

ADEM=Acute disseminated encephalomyelitis; AIS=Acute ischemic stroke; AM=Aseptic meningitis; CHD=Coronary heart disease; CIDP=Chronic inflammatory demyelinating polyneuropathy; DVT=Deep vein thrombosis; EPL=Early pregnancy loss; GBS=Guillain-Barré syndrome; ICH=Intracranial hemorrhage; ITP=Idiopathic or immune thrombocytopenic purpura; KD or KS=Kawasaki's disease or syndrome; MI=Myocardial infarction; MIS-C=Multiple system inflammatory syndrome, in children; MS=Multiple sclerosis; ON=Optic neuritis; PE=Pulmonary embolism; SAB=Spontaneous abortion; SAH=Subarachnoid hemorrhage; SCD=Sudden cardiac death; TIA=Transient ischemic attack; TM=Transverse myelitis; VTE=Venous thromboembolism

ICD-9/10=International Classification of Diseases, 9th/10th Revision; ICD-9-CM=ICD-9, Clinical Modification; H-ICDA=hospital version, International Classification of Diseases, adapted

MIV=Monovalent inactivated influenza vaccine; MMR=Measles, mumps, and rubella; MMRV=Measles, mumps, rubella, and varicella; MMR+V=Separate measles, mumps, and rubella and varicella (vaccines); OPV=Oral poliovirus; Tdap=Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; TIV=Trivalent inactivated vaccine; VZV=Varicella-zoster-containing vaccine; YFV=Yellow fever

ARIC=Atherosclerosis Risk in Communities (study); CDC=Centers for Disease Control and Prevention; DMSS=Defense Medical Surveillance System; NIS=National Inpatient Sample; NVSS=National Vital Statistics System; REP=Rochester Epidemiology Project; VAERS=Vaccine Adverse Event Reporting System; VSD=Vaccine Safety Datalink

CFR=Case fatality rate; IR=Incidence ratio; OR=Odds ratio; HR=Hazard ratio

List of Tables

Table 1. Guillain-Barré syndrome (GBS)

Reference	Population	Total events	Rate				Other measures
			Total	By age group	Males	Females	
NON-VACCINE PUBLICATIONS							
CDC, 2009 [10]	United States	~3000–6000 per year	1–2 per 100,000 population				
Sejvar, et al, 2011 [11] *Meta-analysis of articles from multiple systems 1966–2009*	North America and Europe (N=152.7 million person-years) GBS publications with at least 20 cases and used population-based data; criteria for case definitions of GBS diagnoses	1,643	Crude incidence rate (by study): 0.81–1.89 per 100,000 person-years	0.62–2.66 per 100,000 person-years across all age groups	0–9y: 0.80 10–19y: 0.97 20–29y: 1.18 30–39y: 1.43 40–49y: 1.73 50–59y: 2.09 60–69y: 2.54 70–79y: 3.07 80–89y: 3.72	0–9y: 0.45 10–19y: 0.55 20–29y: 0.66 30–39y: 0.80 40–49y: 0.97 50–59y: 1.18 60–69y: 1.42 70–79y: 1.72 80–89y: 2.09	Relative risk for GBS in males: 1.78 (95% CI: 1.36–2.33)
Shui, et al, 2012 [12] Vaccine Safety Datalink (VSD) 2000–2009	United States Emergency department and inpatient hospitalizations from 7 MCOs among persons with continuous enrollment for 1y (N=50,290,898 person-years) GBS diagnosis via ICD-9 codes	1,619	1.72 per 100,000 person-years*		2.04 per 100,000 person-years*	1.45 per 100,000 person-years*	*Age standardized rate Rates for visits 15% higher in winter and spring compared to summer and fall
Klein, et al, 2010 [13] Electronic record	United States California, northern	121	2.40 per 100,000		Per 100,000	Per 100,000	

review of Northern California Kaiser Permanent study 1998–2004	Among persons 10–62y of age (N=5 million person-years) GBS diagnoses by ICD-9 codes and verified by medical record review		person-years		person-years: 10–17y: 2.1 18–25y: 0.8 26–62y: 3.3	person-years: 10–17y: 1.8 18–25y: 0.4 26–62y: 2.3	
Alshekhlee, et al, 2008 [14] National Inpatient Sample (NIS) 2000–2004	United States Adults ≥18y of age, hospitalized inpatients in NIS facilities (~1,000 hospitals, approximating 20% of US community hospitals) GBS diagnoses by ICD-9-CM codes	4,954	1.65–1.79 per 100,000				In-hospital mortality rate: 2.58%
Myers, et al, 2019 [15] VSD 2004–2015	United States Pregnant women 10–55y of age (N=846,427 person-years or 1,203,624 pregnancies) at 7 managed care organization sites GBS diagnoses via ICD-9 codes and abstraction against Brighton Collaboration case definition for GBS	2	During pregnancy only: 2.8 per million person-years During pregnancy and 42d post-delivery: 2.4 per million person-years				
Salinas, et al, 2017 [16] Hospitalization administrative claims data from island-wide insurance claims database	Puerto Rico Patients from 9 hospitals (population 3,595,839) GBS diagnoses via ICD-9 and ICD-10 codes, compared against Brighton Collaboration case	136	1.7 per 100,000 population				66% with antecedent illness Median time to onset: 7d Most occurred July–September

2013	definition for GBS						
							VACCINE PUBLICATIONS
Wise, et al, 2012 [17] Active, population-based surveillance for incident GBS among 10 Emerging Infections Program (EIP) sites October 2009–May 2010	United States Vaccinated and unvaccinated persons (N=44.9 residents among 10 EIP sites) GBS diagnoses via query to neurologists and healthcare providers; ICD-9 codes from hospital discharge data; all cases compared against Brighton Collaboration case definition for GBS	411	Per 100,000 person-years Overall: 1.38 H1N1 vaccine: 1.85 Seasonal influenza vaccine: 1.73	Per 100,000 person-years: <25y: 0.61 ≥25y: 1.76	52%		Mean interval vaccine-disease: 27d (H1N1) and 36d (seasonal influenza) Estimated 0.74 excess GBS cases per million H1N1 vaccine doses Adjusted rate ratio: 1.57 (95% CI: 1.02-2.21)
Greene, et al, 2012 [18] VSD 2009–2010	United States H1N1 vaccinees followed for development of GBS within 1–42d of vaccination (monovalent inactivated influenza vaccine, MIV, N=1.48 million; seasonal trivalent inactivated influenza vaccine, TIV, N=1.72 million) GBS diagnoses via ICD-9 codes and confirmed by medical record review	MIV: 9 TIV: 8	Relative risk (RR): MIV: 4.4 (95% CI: 1.3–14.2) TIV: 1.3 (95% CI: 0.5–3.8)				Onset: 1-127d (MIV) and 1-84d (TIV)
Polakowski, et al, 2013 [19] Retrospective review of Medicare database October 2009–March 2010	United States 2009 H1N1 vaccine recipients among Medicare beneficiaries hospitalized for GBS (N=3,436,452 doses) GBS diagnoses via ICD-9-CM codes and compared with Brighton Collaboration case definition for GBS	34	Per 100,000 person-years: Onset within 1–42d: 4.30 Onset within 50–119d: 1.83				Attributable risk: 2.47 per 100,000 person-years

Prothro, et al, 2010 [20] EIP October 2009–May 2010	United States Persons residing in 10 state EIP catchment area GBS diagnoses via query to neurologists and healthcare providers; ICD-9 codes from hospital discharge data; all cases compared against Brighton Collaboration case definition for GBS	326	Per 100,000 person-years: Vaccinated: 1.92 Unvaccinated: 1.21				Rate ratio: 1.77 (95% CI: 1.12–2.56) Attributable rate: 0.71 per 100,000 person-years Attributable risk: 0.8 excess GBS cases per 1 million vaccinations
Vellozzi, et al, 2014 [21] EIP October 2009–May 2010	United States Residents of EIP catchment area (N=45 million residents) following vaccination with 2009 monovalent H1N1 vaccine (pH1N1) GBS meeting Brighton Collaboration case definition	Total: 392 Vaccinated: 64	Per 100,000 person-years*: Vaccinated: 1.19 Unvaccinated: 1.43	Per 100,000 person-years (vaccinated / unvaccinated): <25y: 0.54 / 0.67 25–64y: 1.31 / 1.55 ≥65: 2.39 / 2.96	53%		*Age-adjusted rate Vaccinated population had lower risk (Incidence density ratio, IDR=0.83)
Baxter, et al, 2013 [22] Retrospective study of Kaiser Permanente hospital records 1995–2006	United States California, northern Vaccinated and unvaccinated persons in Kaiser Permanente catchment (N=more than 30.2 million person-years) GBS meeting Brighton Collaboration case definition	415	1.27 per 100,000 person-years	Mean age: 48.5y (range: 5–87y)	58.6%		Incidence peaked in winter No increase risk after vaccination In the 90d preceding the onset of GBS, 277 (66.7%) cases had a respiratory or gastrointestinal illness
Filosto, et al, 2020 [23] Observational hospital study March 2020–April 2020	Italy Adults >18y of age followed for GBS and COVID diagnosis in 12 referral hospitals GBS diagnosis per clinical	34 (30 among COVID-positive patients)	Per 100,000 population per year: Overall: 2.43				Compared to 13 cases from April–March 2019 (2019 rate 0.93 per 100,000 population per year), 2.6 fold increase in 2020

	findings and Brighton Collaboration case definition		COVID positive: 2.14 COVID negative: 0.29				Overall GBS incidence per 100,000 population (2019: 0.93 2020: 2.43 Estimated incidence in COVID-19-positive patients: 47.9/100,000 Estimated incidence in COVID-19-positive hospitalized patients: 236/100,000

Table 2. Multiple sclerosis (MS)

Reference	Population	Total events	Rate					Other measures
			Total	By age group	Males	Females	Race/Ethnicity	
NON-VACCINE PUBLICATIONS								
Langer-Gould, et al, 2013 [24] Retrospective cohort of managed care organization 2008–2010	United States California, southern Enrolled members of Kaiser Permanente Southern California health plan (N=9 million person-years) Incident MS diagnoses via ICD-9 codes and confirmed by chart review against standard clinical criteria	496	5.0 per 100,000 person-years	Median age: 41.6y		70.2%	Incidence higher in Black or African American persons and lower in Hispanic/ Latino and Asian and Pacific Islander persons compared with White persons	
Langer-Gould, et al, 2011 [25] *Retrospective cohort of managed care organization 2004–2009*	United States California, southern Enrolled children ≤18y of age of Kaiser Permanente Southern California health plan (N=over 900,000 members)	25	0.51 per 100,000 person-years	Mean age (at onset): 15.6y		64%	Percentage of cases by race/ethnicity: 56% Hispanic/ Latino persons 8% White persons	

							24% Black or African American persons 12% Asian and Pacific Islander persons	
Mayr, et al, 2003 [26] *Rochester Epidemiology Program Project (REP) 1985–2000*	United States Minnesota, Olmsted County		7.5 per 100,000 population*	Per 100,000 population: 0–14y: 0 15–24y: 6.4 25–34y: 12.9 35–44y: 16.7 45–54y: 12.4 55–64y: 2.2 ≥65y: 1.1	Per 100,000 population: Overall: 4.5 0–14y: 0 15–24y: 5.3 25–34y: 4.0 35–44y: 9.4 45–54y: 10.1 55–64y: 3.1 ≥65y: 1.4	Per 100,000 population: Overall: 10.4 0–14y: 0 15–24y: 7.5 25–34y: 21.4 35–44y: 23.7 45–54y: 14.6 55–64y: 1.5 ≥65y: 0.9		*Age- and sex-adjusted Raw prevalence on December 1, 2000: 177 per 100,000 population; prevalence highest among 45–54y olds: 460.0 per 100,000 population
Klein, et al, 2010 [13] *Retrospective study of managed care organization 1998–2004*	United States California, northern Members enrolled in Kaiser Permanente Northern California health plan (N=5 million person-years) MS diagnoses via ICD-9 codes	1,339	14.2 per 100,000 person-years		Per 100,000 person-years: 10–17y: 1.9 18–25y: 2.1 26–62y: 10.0	Per 100,000 person-years: 10–17y: 2.3 18–25y: 8.6 26–62y: 22.9		

Williams, et al, 2017 [27] Defense Medical Surveillance System (DMSS) 2007–2016	United States Active and reserve component members of the Armed Forces and other beneficiaries (e.g., retired service members, family members and dependents) Incident MS via ICD-9 and ICD-10 codes	2,031	14.9 per 100,000 person-years 6.9 per 100,000 persons (reserve/guard members only)	Median age: 32y Per 100,000 person-years: <20y: 4.3 20–24y: 8.5 25–29: 14.4 30–34y: 19.3 35–39y: 25.2 ≥40y: 26.4	11.5 per 100,000 person-years	34.4 per 100,000 person-years	Per 100,000 person-years: Non-Hispanic White persons: 14.8 Non-Hispanic Black or African American persons: 20.3 Hispanic/ Latino persons: 11.3 Other/unknown race: 11.2	Females/Males ratio: 3.7/1 (in 2007)–2.5/1 (in 2016)

Table 3. Transverse myelitis (TM)

Reference	Population	Total events	Rate				Other measures
			Total	By age group	Males	Females	
NON-VACCINE PUBLICATIONS							
Jeffery, et al, 1993 [28] Retrospective analysis of cases from 5 hospitals 1960–1990	United States New Mexico, Albuquerque (N=500,000 people) TM diagnosis via clinical criteria, radiologic features, or cerebrospinal fluid examination	33	4.6 per million per year				45% para-infectious; 21% associated with Multiple sclerosis; 12% associated with spinal cord ischemia; and 21% idiopathic
Sechi, et al, 2019 [29] Rochester Epidemiology Project (REP) 2003–2016	United States Minnesota, Olmsted County (N=153,183 population) TM diagnosis using TM Consortium Working Group diagnostic criteria Incident cases (2013–2016); prevalent cases (December 31, 2016)	Incident: 22 Prevalent: 17 Idiopathic TM: 19	9.49 per 1 million person-years* 8.64 per million popuation*	Median age (at onset): 41y	Per 1 million person-years*: Total: 7.15 0–19y: 0.00 20–39y: 7.37 40–64y: 15.78 ≥65y: 0.00 10.68 per million populatio n*	Per 1 million person-years*: Total: 11.74 0–19y: 0.00 20–39y: 18.07 40–64y: 15.04 ≥65y: 13.91 6.42 per million population* 67% female	*Standardized to world population 3 cases converted to Multiple sclerosis

Klein, et al, 2010 [13] Electronic record review of Northern California Kaiser Permanent study 1998–2004	United States California, northern (N=5 million person-years)	153	3.1 per 100,000 person-years		Per 100,000 person-years: 10–17y: 0.7 18–25y: 0.4 26–62y: 2.4	Per 100,000 person-years: 10–17y: 0.4 18–25y: 1.1 26–62y: 4.9	71% were female, 18–62y of age

Table 4. Optic neuritis (ON)

Reference	Population	Total events	Rate					Other measures
			Total rate	By age group	Males	Females	Race/Ethnicity	
*****NON-VACCINE PUBLICATIONS*****								
Hassan, et al, 2020 [30] Rochester Epidemiology Project (REP) 2000–2018	United States Minnesota, Olmsted County First episode of ON diagnosed based on combination of at least 3 clinical findings	110	Per 100,000 individuals*: ON: 3.9 Multiple sclerosis (MS)-ON: 2.3	Median age (at onset), ON: 37.5y		67%	92% were White persons	*Age- and sex-adjusted rate

Rodriguez, et al, 1995 [31] Population-based study, Mayo Clinic data 1935–1991	United States Minnesota, Olmsted County (N=718,500 person-years) Idiopathic ON diagnosed by clinical criteria; confirmed diagnosis upon review by at least two physicians	37	5.1 per 100,000 person-years* (during 1985–1991)	Median age (at onset): 31y	2.6 per 100,000 person-years	7.5 per 100,000 person-years		*Age- and sex-adjusted rate Age- and sex-adjusted prevalence rate: 115.3 per 100,000 population 39% progressed to MS within 10y diagnosis; 60% within 40y of diagnosis

Table 5. Chronic inflammatory demyelinating polyneuropathy (CIDP)

Reference	Population	Total events	Rate				Other measures
			Total	By age group	Males	Females	
NON-VACCINE PUBLICATIONS							
Laughlin, et al, 2009 [32] Retrospective review of Rochester Epidemiology Project (REP) 1982–2001	United States Minnesota, Olmsted County CIDP diagnosed by clinical criteria followed by review of electrophysiology results	23	1.6 per 100,000 population per year	Median age (range): 58y	(n=13)	(n=10)	Point prevalence on 1/1/2000: 8.9 per 100,000 population
Broers, et al, 2019 [33] Systematic review and meta-analysis 1982–2013	Worldwide 11 studies in systematic review and 5 studies in meta-analysis (N=220,513,514 person-years) Included studies fulfilling general accepted diagnostic criteria for CIDP	818	Pooled crude incidence: 0.33 per 100,000 person-years Crude incidence, by study: 0.15–0.70 per 100,000 person-years		0.51–0.92 per 100,000 population	0.14–0.48 per 100,000 population	Males/Females ratio: 1.5–4.0/1
Querol, et al, 2020 [34] Systematic review and meta-analysis 2009–2019	Worldwide Adults ≥18y of age Diagnoses via general diagnostic criteria for CIDP		Incidence: 0.2–1.6 per 100,000 population				Prevalence: 0.8–8.9 per 100,000 population

Table 6. Acute disseminated encephalitis (ADEM)

Reference	Population	Total events	Rate					Other measures
			Total	By age group	Males	Females	Race/Ethnicity	
NON-VACCINE PUBLICATIONS								
Bhatt, et al, 2019 [35] Retrospective review of National Inpatient Study (NIS) 2006–2014	United States Children ≤18y (N=55,667,114 hospitalizations) Hospitalization for ADEM via ICD-9-CM code in any diagnosis field	3,319	0.5 per 100,000 population By year (p<0.001) 2006–2008: 0.4 2009–2011: 0.5 2012–2014: 0.6	Median age: 6y Peak incidence: 2y Children 0–4y: 0.7 per 100,000 population	0.5 per 100,000 population	0.5 per 100,000 population	Black or African American and Hispanic or Latino children with significantly increased risk Per 100,000 population: Black or African American persons: 0.3 Hispanic or Latino persons 0.4 White persons: 0.3	67% of ADEM hospitalizations in children <9y Highest incidence in spring Temporal increase p-trend <0.001 (2006/8 to 2012/14)
Leake, et al, 2004 [36] Retrospective and prospective study 3 principal pediatric hospitals 1991–2000	United States California, San Diego County Children <20y (N=855,633 population)	42	0.4 per 100,000 persons per year	Median age: 6.5y Per 100,000 persons per year: 0–4y: 0.6 5–9y: 0.8		43%		Two (5%) of patients received vaccinations within 21 days of ADEM illness onset 66% cases occurred during 1998–2000
VACCINE PUBLICATIONS								
Pellegrino, et al, 2015 [37] Vaccine Adverse	United States Influenza vaccinated population	Seasonal influe	Seasonal influenza: 0.05					Seasonal influenza by year: 0.03 per 1

Event Reporting System (VAERS) 2006–2014	Diagnosis of ADEM following vaccination against seasonal influenza (2006–2014) and H1N1 (2013–2014) vaccination	nza: 60 H1N1: 12	per 1 million doses H1N1: 0.15 per 1 million doses					million doses in 2011–2012 and 0.09 per 1 million doses in 2007–2008

Table 7. Aseptic meningitis (AM)

Reference	Population	Total events	Rate				Other measures
			Total	By age group	Males	Females	
							NON-VACCINE PUBLICATIONS
Nicolosi, et al, 1986 [38] Mayo Clinic and private provider medical records for medical encounters in patients from Olmsted County, Minnesota 1950–1981	United States Minnesota Persons of Olmsted County, MN seeking medical care at affiliated hospitals and clinics AM defined as a benign, self-limiting disease without evidence of brain parenchymal involvement and included fever, headache, and other signs of meningeal pleocytosis of the CSF; the term AM used to indicate viral or presumed viral meningitis	1950–1981: 283 1976–1981: 101	1950–1981: 10.9 per 100,000 person-years* 1976–1981: 17.8 per 100,000 person-years*	Per 100,000 person-years* <1y: 82.4 1–4y: 16.2 5–9y: 18.8 10–19y: 14.5 20–29y: 15.8 30–39y: 10.5 40–59y: 1.4 ≥60y: 0.7	Per 100,000 person-years* Total: 13.1 <1y: 92.5 1–4y: 21.8 5–9y: 22.3 10–19y: 18.3 20–29y: 18.2 30–39y: 12.1 40–59y: 1.4 ≥60y: 1.7	Per 100,000 person-years* Total: 8.7 <1y: 71.2 1–4y: 10.4 5–9y: 15.1 10–19y: 10.0 20–29y: 14.1 30–39y: 8.9 40–59y: 1.3 ≥60y: N/A	*Age- and sex-adjusted incidence rates
							VACCINE PUBLICATIONS
Black, et al, 1997 [39] Vaccing Safety Datalink (VSD) case-control study 1992–1993	United States Vaccinated children 12–23m of age, hospitalized in four health maintenance organizations (~500,000 children under 7y of age under	59	16.9 per 100,000 person-years* (95% CI: 12.5–21.2)				*8.7 (95% CI: 0.2–48.5) per 100,000 person-years within 14d of vaccination *12.2 (95% CI: 2.5–35.6) per 100,000 person-

	surveillance) for AM 0–14d after MMR with Jeryl-Lynn mumps strain AM defined by ICD-9 codes from discharge diagnoses, cases underwent further medical records review against a predifined case definition excluding other causes of meningitis						years within 30d of vaccination

Table 8. Encephalitis

Reference	Population	Total events	Rate					Other measures
			Total	By age group	Males	Females	Race/ethnicity	
NON-VACCINE PUBLICATIONS								
Vora, et al, 2014 [40] NIS 1998–2010	United States NIS (N=8 million hospitalizations per year) Hospitalizations for encephalitis, diagnosis via ICD-9-CM codes	263,352 (20,258 per year)	6.9 per 100,000 persons per year	Per 100,000 persons per year: <1y: 11.1 1–4y: 4.7 5–19y: 4.0 20–44y: 5.7 45–64y: 8.4 ≥65y: 13.2	6.6 per 100,000 persons	7.2 per 100,000 persons		Etiology: 5.5% post-infectious HIV in 8.8% of hospitalizations, viral pathogens in 20.3% of hospitalizations
George, et al, 2014 [41] Retrospective observational study of Nationwide Inpatient Sample (NIS) 2000–2010	United States NIS (N=8 million hospitalizations in non-federal acute care hospitals per year) Hospitalizations for encephalitis, diagnosis via ICD-9 codes	238,567	Per 100,000 population: Overall: 7.3 Post-immunization: 0.01–0.02 Post-infectious: 0.26–0.44	Mean age: 44.8y Per 100,000 population: <1y: 13.5 1–4y: 5.1 5–19y: 4.4 20–44y: 5.9 45–64y: 8.7 ≥65y: 14.1	7.0 per 100,000 population	7.6 per 100,000 population		Etiology: 25.6% viral, 50% unknown 7.7% with comorbid HIV/AIDS and 6.8 % with comorbid cancer

Dubey, et al, 2018 [42] Rochester Epidemiology Project (REP) 1995–2015	United States Minnesota, Olmsted County (N=155,284 population) Autoimmune and infectious or viral encephalitis using established criteria for diagnosis	Autoimmune: 24 Infectious: 28 Viral: 18	Per 100,000 person-years: Autoimmune: 0.8 Infectious: 1.0 Viral: 0.6 ADEM: 0.1	Median age (at onset): 43y		Autoimmune: 36% Infectious: 69%	Autoimmune encephalitis rates, per 100,000 person-years: Black or African American persons: 2.8 White persons: 0.7	Autoimmune encephalitis (1995-2005): 0.4/100,000 PY (2006-2015): 1.2/100,000 PY
*****VACCINE PUBLICATIONS*****								
Pahud, et al, 2012 [43] Review of immunization records and case-centered methodology from California Encephalitis Project (CEP) July 1998–December 2008	United States California Children 6m–18y of age followed for encephalitis (n=110) with varying risk windows depending upon vaccine received Encephalitis per criteria and immunization in 1y period preceding diagnosis	110	Odds ratio (OR) (by risk window): 42d (31 cases): 1.03 30d (23 cases): 0.94 21d (20 cases): 1.21					Measles-containing vaccines (n=36): 5–15d, 2 cases, OR: 1.31 Pertussis-containing vaccines (n=62) 0–3d,1 case, OR: 1.37 Conclusion: no association with vaccination found

Table 9. Seizures (epilepsy and first unprovoked seizure)

Reference	Population	Total events	Rate					
			Total	By age group	Males	Females	Race/Ethnicity	
NON-VACCINE PUBLICATIONS								
Hauser, et al, 1993 [44] Rochester Epidemiology Project (REP) 1935–1984	United States Minnesota, Rochester Residents seen in area medical facilities (N=2 million person-years) Epilepsy was defined as recurrent unprovoked seizures (or seizures without an identified proximate precipitant); individuals with a single unprovoked seizure were categorized separately. Clusters of seizures in single 24h period were categorized as a single seizure episode	Epilepsy: 880 First unprovoked seizure: 1,208	Per 100,000 person-years*: Epilepsy: 44 First unprovoked seizure: 61	Per 100,000 person-years (epilepsy†): 0–1y: 86 1–4y: 62 5–9y: 50 10–14y: 39 15–19y: 44 20–24y: 39 25–29y: 30 30–34y: 23 35–39y: 33 40–44y: 26 45–49y: 23 50–54y: 31 55–59y: 32 60–64y: 40 65–69y: 55 70–74y: 88 75–79y: 111 80–84y: 158 ≥85y: 180	Per 100,000 person-years*: Epilepsy: 49 First unprovoked seizure: 68	Per 100,000 person-years*: Epilepsy: 41 First unprovoked seizure: 56		*Age-adjusted incidence rates; adjusted to 1970 US population Incidence rates available by type of seizure and etiology †Trends in age-specific incidence of first unprovoked seizure were similar to epilepsy and highest in older age groups
Benn, et al, 2008 [45] Population-based study of northern Manhattan residents seen	United States New York Low-income, predominantly Hispanic community in Northern Manhattan, New York City	Epilepsy: 82 First unprovoked seizure: 209	Per 100,000 person-years*: First unprovoked seizure: 46.6 per 100,000 person-years*	Per 100,000 person-years: First unprovoked seizure: <1y: 134.4	First unprovoked seizure: 46.6 per 100,000 person-years*	First unprovoked seizure: 35.9 per 100,000 person-years*	First unprovoked seizure, Per 100,000 person-years: Hispanic	*Age- and sex-adjusted incidence rates Incidence rates available by type

at area hospitals and nursing homes 2003–2005	Epilepsy was defined as recurrent unprovoked seizures (or seizures without an identified proximate precipitant); individuals with a single unprovoked seizure were categorized separately. Clusters of seizures in single 24h period were categorized as a single seizure episode		Epilepsy: 16.4 First unprovoked seizure: 41.1	1–4y: 50.4 5–9y: 41.5 10–14y: 30.7 15–24y: 39.8 25–34y: 13.1 35–44y: 21.3 45–54y: 31.5 55–64y: 35.3 65–74y: 45.3 75–84y: 144.7 ≥85y: 235.5			persons: 36.5 Non-Hispanic white persons: 39.4 Non-Hispanic Black or African American persons: 37.6 Non-Hispanic other race: 50.3	of seizure and etiology
Annegers, et al, 1999 [46] Retrospective review of health maintenance organization medical records 1988–1994	United States Texas Patients enrolled in Kelsey-Seybold Clinics in Houston, a health maintenance organization covering a multi-ethnic, urban population <65y of age (N=600,000 person-years) Epilepsy was defined as recurrent unprovoked seizures (or seizures without an identified proximate precipitant). Cases initially identified in medical records using ICD-9 codes	Epilepsy: 197 First unprovoked seizure: 275	Per 100,000 person-years: Epilepsy: 35.5 First unprovoked seizure: 50.9	Per 100,000 person-years: Epilepsy: <5y: 67.0 5–14y: 59.6 15–24y: 45.0 25–34y: 17.5 35–44y: 14.1 45–54y: 12.4 55–64y: 20.9 65–74y: 20.3 ≥75y: 0.0 First unprovoked seizure: <5y: 93.5 5–14y: 79.7 15–24y: 59.6 25–34y: 23.3 35–44y: 20.0 45–54y: 24.8 55–64y: 36.5 65–74y: 64.0 ≥75y: 99.2	Per 100,000 person-years: Epilepsy: <5y: 51.8 5–14y: 64.9 15–24y: 53.1 25–34y: 20.2 35–44y: 10.3 45–54y: 15.8 55–64y: 16.7 65–74y: 0.0 ≥75y: 0.0 First unprovoked seizure: <5y: 76.0 5–14y: 84.7 15–24y:	Per 100,000 person-years: Epilepsy: <5y: 82.9 5–14y: 54.0 15–24y: 39.7 25–34y: 15.9 35–44y: 16.8 45–54y: 9.7 55–64y: 24.5 65–74y: 41.9 ≥75y: 0.0 First unprovoked seizure: <5y: 111.7 5–14y: 74.5 15–24y: 48.5 25–34y: 23.9 35–44y: 22.4 45–54y: 24.3 55–64y: 39.2 65–74y: 54.3 ≥75y: 182.8	Incidence rates by ethnicity did not differ	Conclusion: the lower incidence rates in the study population likely because of a healthy-worker effect (lower risk than general population)

					76.3 25–34y: 22.5 35–44y: 16.4 45–54y: 25.3 55–64y: 33.4 65–74y: 72.6 ≥75y: 0.0			

Table 10. Cerebrovascular accident (stroke), ischemic and hemorrhagic

Reference	Population	Total events	Rate	Other measures				
			Total	By age group	Males	Females	Race/Ethnicity	
								NON-VACCINE PUBLICATIONS
Koton, et al, 2020 [47] Community-based prospective Atherosclerosis Risk in Communities (ARIC) Cohort Study 1987–2017	United States Multiple sites Participants (N=14,357 persons, 55% female, median age 54.1y; N=326,654 person-years) free of stroke at baseline (1987–1989) and followed through December 31, 2017 for stroke hospitalization Possible strokes identified via ICD-9 codes; incident strokes defined as first definite or probable stroke without self-report of physician-diagnosed stroke at baseline	1,340	4.10 per 1,000 person-years*	Per 1,000 person-years*: <65y: 2.19 (312 strokes in 142,312 person-years) ≥65: 5.58 (1,028 strokes in 184,343 person-years)	4.59 per 1,000 person-years* (635 strokes in 138,336 person-years)	3.74 per 1,000 person-years* (705 strokes in 188,318 person-years)	Per 1,000 person-years*: White persons: 3.39 (834 strokes in 245,931 person-years) Black or African American persons: 6.26 (506 strokes in 80,823 person-years)	*Crude incidence rates
Koton, et al, 2014 [48]	United States	Total:	Per 1,000	Per 1,000	4.28	3.31	Per 100,000	*Crude incidence

ARIC Study 1987–2011	Participants (N=14,357 persons or N=282,097 person-years) 45–64y of age at baseline (1987–1989) followed through December 31, 2011 for incident stroke Incident stroke defined as a first definite or probable stroke in a participant with no physician-diagnosed stroke at the baseline interview	1,051 Ischemic: 929 Hemorrhagic: 140	person-years*: Total: 3.73 (95% CI: 3.51–3.96) Ischemic: 3.29 (95% CI: 3.08–3.50) Hemorrhagic: 0.49 (95% CI: 0.41–0.57)	person-years*: <65y: 2.19 (95% CI: 1.96–2.45) (312 strokes in 142,303 person-years) ≥65y: 5.29 (95% CI: 4.92–5.68) (739 strokes in 139,795 person-years) During follow-up in 2008–2011: 60–64y: 5.9 65–69y: 2.1 70–74y: 4.4 75–79y: 6.8 80–85y: 8.8 During follow up in 1990–1992: 45–49y: 1.2 50–54y: 1.7 55–59y: 2.4 60–64y: 3.1 65–69y: 3.1	per 1,000 person-years* (95% CI: 3.93–4.67) (518 strokes in 120,967 person-years)	per 1,000 person-years* (95% CI: 3.04–3.60) (533 strokes in 161,130 person-years)	person-years: White persons: 2.96 (95% CI: 2.74-3.20) (626 strokes in 211,452 person-years) Black or African American persons: 6.02 (95% CI: 5.47-6.62) (425 strokes in 70,645 person-years)	rates
Tong, et al, 2016 [49] National Inpatient Sample (NIS) of the Healthcare Cost and Utilization Project	United States Adults ≥18y of age at the time of hospitalization, followed for			In 2011–2012, per 100,000 persons: 18–34y:				

(HCUP) 2003–2012	stroke hospitalizations Stroke identified by ICD-9-CM codes for subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), and acute ischemic stroke (AIS)			SAH: 2.33 ICH: 1.97 AIS: 6.95 35–44y: SAH: 6.51 ICH: 6.37 AIS: 34.87 45–54y: SAH: 12.82 ICH: 18.51 AIS: 114.76 55–64y: SAH: 15.46 ICH: 29.45 AIS: 263.90 65–74y: SAH: 15.90 ICH: 48.40 AIS: 537.17 75–84y: SAH: 22.82 ICH: 116.44 AIS: 1,127.09 ≥85y: SAH: 27.09 ICH: 179.12 AIS: 1,703.66				
Madsen, et al, 2017 [50] Data from the Greater Cincinnati/Northern	United States Greater Cincinnati and Northern Kentucky Residents (N=1.3	Males: 840 Females: 1,101			Per 100,000 population*: Total: 192	Per 100,000 populatio n*:		*Adjusted incidence rates were standardized to the year 2000 US census population

Kentucky Stroke Study (GCNKSS) 2010	million) ≥20y of age at all local hospitals First-ever strokes (ischemic, ICH, and SAH) identified by ICD-9 codes in hospitalized records, or ascertained through records from regional public health clinics, outpatient clinics, coroner's offices; all cases verified by study physician				Ischemic: 165 ICH: 34 SAH: 5	Total: 198 Ischemic: 173 ICH: 25 SAH: 10		Additional rates are available by stroke type for 1993–1994, 1999, 2005 Case fatality rates (CFR) (males / females): All strokes: 13% / 12.6% Ischemic stroke: 8.5% / 9.5% ICH: 36.7% / 37.9% SAH: 16.1% / 26.8%
White, et al, 2005 [51] Population-based stroke surveillance Northern Manhattan Study (NOMAS) July 1993–June 1997	United States Northern Manhattan (N=210,000) Residents ≥20y of age in area for ≥3m First ischemic stroke defined by National Institute of Neurological Disorders and Stroke	714					Per 100,000 population*: White persons: 88 Black or African American persons: 191 Hispanic persons: 149	*Age-adjusted annual incidence rate Conclusion: higher ischemic stroke incidence among Black or African American persons and Hispanic persons, compared with White persons, for all types of ischemic strokes
Zahuranec, et al, 2014 [52] *Population-based stroke surveillance*	United States Texas, Nueces County Adults ≥45y of	734	In 2010: 4.30 per 10,000					*Age-, sex-, and ethnicity-adjusted rate

(Brain Attack Surveillance in Corpus Christi, BASIC) from National Institute of Neurological Disorders and Stroke (NINDS) 2000–2010	age (2000, N=45,984 Mexican Americans (M-A) and 49,540 non-Hispanic White (NHW); 2010, N=66,125 M-A and 55,779 NHW) Intracerebral hemorrhage diagnoses via ICD-9 codes, validated by neurologists		population * (95% CI: 3.21–5.76)					
Morgenstern, et al, 2013 [53] BASIC/NINDS 2000–2010	United States Texas, Nueces County Adults ≥45y of age (2000, N=45,984 Mexican American persons (M-A) and 49,540 non-Hispanic White persons (NHW); 2010, N=66,125 M-A and 55,779 NHW) First ischemic stroke, validated by neurologists blinded to ethnicity and age	Total: 4,646 (M-A: 2,604, NHW: 2,042)					Per 10,000 population, in 2010 (NHW / M-A): 45–59y: 6.5 / 13.1 60–74y: 15.9 / 23.7 ≥75y: 49.7 / 52.4	Incidence rate ratio comparing M-A to NHW, for first ischemic stroke: 45–59y: 1.94 60–74y: 1.50 ≥75y: 1.00 Conclusion: M-A <75y may have higher rates of stroke compared with NHW
Zhang, et al, 2008 [54] Longitudinal,	United States American Indian or Alaska Native	306	679 per 100,000	Mean age: 66.5y			Conclusion: compared to rates from	*Age- and sex-adjusted incidence rate

population-based, observational Strong Heart Study 1989–2004	participants (N=4,507) without a prior stroke, 45–74y of age at enrollment		person-years*				previous studies of White and Black or African American persons, American Indian persons have higher incidence and case-fatality for first stroke, in same age-range	86% of incident strokes were ischemic
Agrawal, et al, 2009 [55] Retrospective review of Kaiser Permanente, Northern California out- and inpatient electronic records 1997–2003	United States Kaiser Permanente, Northern California Children <20y of age (N=2,347,982) Stroke diagnoses via ICD-9 codes, radiology reports suggestive of infarction; cases confirmed through chart review	Ischemic: 132 Hemorrhagic: 114 Transient ischemic attacks: 7	Per 100,000 person-years: Ischemic: 2.4 Ischemic + hemorrhagic: 4.6	Ischemic, perinatal: 29 per 100,000 live births (1 per 3,500 live births) Ischemic, later-childhood*: 1.3 per 100,000 person-years				*Excludes perinatal period
Fullerton, et al, 2003 [56] Retrospective review of hospital discharge data from California-wide hospital discharge database 1991–2000	United States California Children 1m–19y First admissions for stroke	2,278	Per 100,000 children per year: Total: 2.3 Ischemic:		Per 100,000 children per year: All strokes: 2.57 ICH: 0.87	Per 100,000 children per year: All strokes: 2.02	Per 100,000 children per year: All strokes White children: 1.99 Black or African American	After eliminating cases with coexisting sickle cell disease, excess stroke risk persisted in Black or African American children Boys higher risk for

			1.2 Hemorrhagic: 1.1		SAH: 0.4 Ischemic: 1.30	ICH: 0.65 SAH: 0.32 Ischemic: 1.05	children: 4.22 Hispanic children: 1.50 Asian children: 1.90 ICH White children: 0.67 Black or African American children: 1.11 Hispanic children: 0.52 Asian children: 0.71 SAH White children: 0.30 Black or African American children: 0.48 Hispanic children: 0.28 Asian children: 0.23 Ischemic White children: 1.01 Black or African American children: 2.62 Hispanic children: 0.71 Asian children: 0.96	all stroke types than girls; after elimination of trauma, excess stroke risk persisted in boys Compared with girls, boys had a higher case fatality rate for ischemic stroke

								VACCINE PUBLICATIONS
Klaric, et al, 2019 [57] *A Cox proportional hazards regression model of data from cross-sectional Behavioral Risk Factors Surveillance System (BRFSS) 2014*	United States Self-reported live attenuated Zoster (Zostavax) vaccination status from N=265,568 respondents 50–79y of age Self-reported history of stroke Comparing those without vaccination to those with vaccination		Hazard ratio (HR): 1.73 (95% CI: 1.71–1.76)	Odds ratio (OR): 65–69y: 1.51 (95% CI: 1.21–1.88)				Conclusion: those without Zoster vaccination are at significantly higher risk for stroke compared to those receiving zoster vaccination. In remaining 5-year age groups beyond age 50y, respondents with and without zoster vaccination are as likely to report strokes
Donahue, et al, 2009 [58] *Vaccine Safety Datalink (VSD) 1991–2004*	United States Children 11m–17y of age, enrolled for ≥12m in 8 managed care organizations (N=3.25 million); 35.3% of population vaccinated with Varicella vaccine Ischemic stroke diagnoses via ICD codes, not verified by chart review	203	Ischemic stroke rate: 1.2 per 100 000 person-years Adjusted HR by time since vaccination: <1m: 1.1 (95% CI: 0.1–9.2) 1–3m: 0.7 (95% CI:					Conclusion: varicella vaccination is not associated with ischemic stroke in children. Stroke was strongly associated with known risk factors (e.g., sickle cell disease and cardiac disease).

			0.1–5.7) 3–6m: 1.3 (95% CI: 0.3–5.6) 6–9m: 1.3 (95% CI: 0.4–4.9 9–12m: 0.4 (95% CI: 0.0–3.2)					

Table 11. Narcolepsy and cataplexy

Reference	Population	Total events	Rate				Other measures
			Total	By age group	Males	Females	
NON-VACCINE PUBLICATIONS							
Silber, et al, 2002 [60] Rochester Epidemiology Project (REP) 1960–1989	United States Minnesota, Olmsted County N=2,558,169 person-years Narcolepsy cases (with and without cataplexy) identified via H-ICDA diagnostic codes and subsequently reviewed against Mayo classification criteria	35 (narcolepsy with and without cataplexy)	1.37 per 100,000 persons per year	Per 100,000 persons per year: 0–9y: 1.01 10–19y: 3.84 20–29y: 1.84 30–39y: 1.06 40–49y: 0.00 50–59y: 0.47 60–69y: 0.00 70–79y: 0.00 80–89y: 0.00 90–99y: 0.00 100–109y: 0.00	Per 100,000 persons per year: Overall: 1.72 0–9y: 1.97 10–19y: 4.56 20–29y: 0.52 30–39y: 2.13 40–49y: 0.00 50–59y: 0.97 60–69y: 0.00 70–79y: 0.00 80–89y: 0.00 90–99y: 0.00 100–109y: 0.00	Per 100,000 persons per year: Overall: 1.05 0–9y: 0.00 10–19y: 3.13 20–29y: 2.87 30–39y: 0.00 40–49y: 0.00 50–59y: 0.00 60–69y: 0.00 70–79y: 0.00 80–89y: 0.00 90–99y: 0.00 100–109y: 0.00	Total rate for narcolepsy with cataplexy 0.74 per 100,000 persons per year; age- and sex-specific rates also provided

Table 12. Myocarditis and pericarditis

Reference	Population	Total events	Rate					Other measures
			Total	By age group	Males	Females	Race/Ethnicity	
NON-VACCINE PUBLICATIONS								
Manda and Baradhi, 2020 [61] Review article	Acute myocarditis		1–10 per 100,000 per year					Acute pericarditis: 0.1% of hospital admissions
Kumar, et al, 2016 [62] Nationwide Inpatient Sample (NIS) 2003–2012	United States Persons ≥16y of age Acute pericarditis diagnoses via ICD-9 codes	28,496 hospitalizations (representing 135,710 hospitalizations nationally)	57.3 per 1 million person-years	Mean age: 53.5y Per 1 million population (in 2012): Overall: 54 16–49y: 37 50–64y: 68 65–74y:85 75–84y:92 ≥ 85y: 87	67 per 1 million population (in 2012)	41 per 1 million population (in 2012)		Acute pericarditis hospitalization male/female Incidence rate ratio (IRR): 1.56

Mody, et al, 2018 [63] Center for Medicare and Medicaid Services (CMS), inpatient Standard Analytical files 1999–2012	United States Medicare fee-for-service beneficiaries ≥65y of age Hospitalization for acute pericarditis, diagnoses via ICD-9-CM codes	45,504	26.0 per 100,000 person-years	Per 100,000 PY (2012): 68-74y: 23 75-84y: 31 ≥85y: 27	27.0 per 100,000 PY (2012)	25.0 per 100,000 PY (2012)	Per 100,000 PY (2012): White persons: 26.0 Black or African American persons: 29.0	
Lin, et al, 2013 [64] Review of Military hospital and cardiology clinic records 2004–2008	United States Armed service members deployed to Iraq and Kuwait (N=189,118) Acute pericarditis and myopericarditis using established clinical criteria	Pericarditis: 70 Myopericarditis: 9	Per 100,000 population per year: Pericarditis: 7.4 Myopericarditis: 0.95	Mean age: 31.3y				11 with Smallpox vaccination 4–30d prior to onset Mean onset: 28.3d post-vaccination 11 of 79 (14%) cases of pericarditis and myopericarditis received smallpox vaccine 4-30 days prior to diagnosis
								*****VACCINE PUBLICATIONS*****
Halsell, et al, 2003 [65] Defense Medical Surveillance	United States Military service members following Smallpox (vaccinia) vaccination	Primary vaccinees: 18	7.8 per 100,000 vaccinees over 30d					All cases occurred among white men 21–33y of age (mean:

System (DMSS) and Vaccine Adverse Event Reporting System (VAERS) December 2002–March 2003	(N=326,356 vaccinees of which 95,622 were revaccinated and 230,734 were primary vaccinees) Myopericarditis in 30d following vaccination via ICD-9 codes		2.16 per 100,000 (all service men on active duty) over 30d					26.5y) Presented 7–19d post-vaccination (mean: 10.5d) Myopericarditis 3.6 times higher in primary vaccinees compared to unvaccinated individuals
Arness, et al, 2004 [66] DMSS or VAERS December 2002–September 2003	United States Armed Forces personnel following smallpox vaccination (N=492,671) Myo- and pericarditis via ICD-9 codes	59 (56 among primary vaccinees)	Per 100,000 vaccinees*: Primary vaccinees: 16.11 Re-vaccinees: 2.07		98.3%		White persons: 86.4%	*Compared with expected rate: 2.16 per 100,000 non-vaccinated persons Onset: 2–29d post-vaccination
Morgan, et al, 2008 [67] Active and passive surveillance systems for adverse events (including, VAERS) January–October 2003	United States Civilians post-smallpox vaccination (N=37,901 vaccinees) Myopericarditis within 6w of vaccination; case definition: VAERS codes and chart	21	5.5 per 10,000 vaccinees	Median age: 48y		67%		86% were re-vaccinees Median time to onset: 11d (range: 2–42d)

	review meeting diagnostic criteria							
Kuntz, et al, 2018 [68] Vaccine Safety Datalink (VSD) Self-controlled Risk Interval (SCRI) study 1996–2007	United States Vaccinated adults ≥18y of age (N=416,629) at Kaiser Permanente sites Vaccines: MMR, VZV, OPV, YFV live viral vaccines Diagnoses of pericarditis and myopericarditis in 42d following vaccination via ICD-9 codes	Pericarditis: 1 Myocarditis: 0	Myocarditis: 0.24 per 100,000 vaccinated persons					

Table 13. Venous thromboembolism (VTE)

Reference	Population	Total events	Rate				Other measures
			Total	By age group	Males	Females	
NON-VACCINE PUBLICATIONS							
Huang, et al, 2014 [69] Population-based study of Worcester, Massachusetts, metropolitan statistical area residents 1985–2009	United States Massachusetts 5,025 residents of Worcester, MA metropolitan statistical area VTE diagnoses based on ICD-9	5,025	Per 100,000 population per year: Overall: 108 In 2009: 133	Mean age: 65 ± 18y	46%		Rates increased over the 25-year study period
Silverstein, et al, 1998 [70] Population-based inception cohort 1966–1990	United States Minnesota, Olmsted County Residents (1990 population 106,470) First time VTE based upon clinical case definition	2,218	117 per 100,000 population per year*		130 per 100,000 population per year† 0–14y: 1 15–19y: 10 20–24y: 29 25–29y: 25 30–34y: 39 35–39y: 45 40–44y: 80 45–49y: 88 50–54y: 136 55–59y: 157 60–64y: 299 65–69y: 384 70–74y: 702 75–79y: 632 80–84y: 1,146 ≥85y: 919	110 per 100,000 population per year† 0–14y: 0.3 15–19y: 27 20–24y: 51 25–29y: 72 30–34y: 75 35–39y: 74 40–44y: 84 45–49y: 96 50–54y: 123 55–59y: 122 60–64y: 207 65–69y: 249 70–74y: 351 75–79y: 514 80–84y: 703 ≥85y: 965	*Incidence rate is age- and sex-adjusted †Incidence rate is age-adjusted

Beckman, et al, 2010 [71] Analyses of clinical administrative databases and hospital- and community-based studies	United States Total US population	900,000 per year	1–2 per 1,000 population per year	Per 1,000 population per year: <15y: <0.5 15–44y: 1.49 45–79: 1.92 ≥80y: 5–6	1.3 per 1,000 population per year	1.1 per 1,000 population per year	10–30% mortality within 30 days
Stein, et al, 2004 [72] Data from the National Hospital Discharge Survey and the United States Bureau of the Census 1979–2001	United States Hospitalized patients in the US and District of Columbia VTE diagnoses based on ICD-9-CM for Pulmonary embolism (PE) and deep vein thrombosis (DVT)	8,575,000	113–167 per 100,000 population per year		104–148 per 100,000 population per year	123–185 per 100,000 population per year	PE mortality 2.5–4.5 per 100,000 population per year (1979–1998)

Table 14. Myocardial infarction (MI), acute

Reference	Population	Total events	Rate				Other measures
			Total	By age group	Males	Females	
							NON-VACCINE PUBLICATIONS
Virani, et al, 2020 [73] 2020 update of Heart Disease and Stroke Statistics, Unpublished National Heart, Lung, and Blood Institute tabulation using Atherosclerosis Risk in Communities (ARIC) study and Cardiovascular Health Study (CHS) data 2005–2014	United States First and recurrent MI	805,000 per year (age ≥35y)			Average age: 65.6y Per 1,000 person-years White persons: 35–44y: 0.8 45–54y: 2.1 55–64y: 3.8 65–74y: 7.3 75–84y: 9.4 Black or African American persons: 35–44y: 2.4 45–54y: 4.0 55–64y: 7.1 65–74y: 10.7 75–84y: 15.9	Average age: 72.0y Per 1,000 person-years White persons: 35–44y: 0.3 45–54y: 1.0 55–64y: 2.1 65–74y: 3.7 75–84y: 8.5 Black or African American persons: 35–44y: 1.1 45–54y: 2.7 55–64y: 4.4 65–74y: 7.7 75–84y: 12.0	Mortality from diagnosed heart attack or fatal CHD (*per 1,000 adults diagnosed with MI or CHD): Males: 35–44y: 25 45–54y: 75 55–64y: 130 65–74y: 155 75–84y: 135 ≥85y: 90 Females: 35–44y: 10 45–54y: 40 55–64y: 70 65–74y: 90 75–84y: 110 ≥85y: 125
							VACCINE PUBLICATIONS
Tseng, et al, 2010 [74] Kaiser Permanente prospective study Automated data 2002–2007	United States California California Men's Health Study participants aged 45–69y (N=84,170) in 2 managed care organizations prospectively followed for first MI events after pneumococcal polysaccharide	1,211	10.73 per 1,000 person-years		10.73 per 1,000 person-years		Conclusion: found no evidence for an association between pneumococcal vaccination and reduced risk of acute MI,

	vaccination (112,837 vaccinated person-years) MI diagnosis via ICD-9 (medical encounters) and ICD-10 (mortality records)						adjusted Hazard Ratio (HR) 1.09 (95% CI: 0.98–1.21)
Jackson, et al, 2002 [75] Group Health Cooperative (GHC), Washington Population-based inception cohort study 1992–1996	United States Washington GHC population, includes >400,000 covered residents of western Washington State Survivors aged 30–79y of first MI receiving each year's influenza vaccine (N=1,378) with aim to assess risk of recurrent MI and death from atherosclerotic cardiovascular disease following influenza vaccination MI diagnosis via ICD-9	127 recurrent coronary events in a median 2.3-year study period	127 per 3,267 person-years				Influenza vaccination was not associated with risk of recurrent coronary events during November–October (adjusted HR: 1.18, 95% CI:0.79-1.75)

Table 15. All-cause, cause-specific mortality

Reference	Population	Event	Rate				Other measures
			Total	By age group	Males	Females	
							NON-VACCINE PUBLICATIONS
CDC, 2018 [76] *CDC's National Vital Statistics System (NVSS) 2017*	United States (50 states and District of Columbia)	All causes	863.8 per 100,000 population*	Per 100,000 population: 1–4y: 24.3 5–14y: 13.6 15–24y: 74.0 25–34y: 132.8 35–44y: 195.2 45–54y: 401.5 55–64y: 885.8 65–74y: 1,790.9 75–84y: 4,472.6 ≥85y: 13,573.6	Per 100,000 population: Total: 897.2 1–4y: 27.3 5–14y: 15.6 15–24y: 106.1 25–34y: 183.3 35–44y: 249.4 45–54y: 496.5 55–64y: 1,112.3 65–74y: 2,190.2 75–84y: 5,254.0 ≥85y: 14,689.2	Per 100,000 population: Total: 831.4 1–4y: 21.1 5–14y: 11.4 15–24y: 40.4 25–34y: 80.8 35–44y: 141.4 45–54y: 309.0 55–64y: 674.7 65–74y: 1,440.4 75–84y: 3,869.1 ≥85y: 12,966.5	*Rate is age-adjusted
		Deaths caused by diseases of heart (I00–I09, I11, I13, I20–I51)	198.8 per 100,000 population*	Per 100,000 population: 1–4y: 0.8 5–14y: 0.4 15–24y: 2.1 25–34y: 8.1 35–44y: 25.4 45–54y: 77.1 55–64y: 190.7 65–74y: 392.9 75–84y: 1,028.4 ≥85y: 3,882.9	Per 100,000 population: Total: 216.9 1–4y: 0.8 5–14y: 0.5 15–24y: 2.8 25–34y: 10.7 35–44y: 34.7 45–54y: 109.1 55–64y: 273.2 65–74y: 538.5 75–84y: 1,306.8 ≥85y: 4,421.1	Per 100,000 population: Total: 181.2 1–4y: 0.8 5–14y: 0.4 15–24y: 1.4 25–34y: 5.5 35–44y: 16.2 45–54y: 45.9 55–64y: 113.9 65–74y: 265.1 75–84y: 813.5 ≥85y: 3,589.9	
		Deaths caused by	44.9 per 100,000	Per 100,000 population:	Per 100,000 population:	Per 100,000 population:	

		cerebrovascular disease (I60–I69)	population*	1–4y: 0.4 5–14y: 0.2 15–24y: 0.4 25–34y: 1.3 35–44y: 4.4 45–54y: 12.3 55–64y: 30.3 65–74y: 76.4 75–84y: 263.1 ≥85y: 993.5	Total: 38.4 1–4y: 0.5 5–14y: 0.3 15–24y: 0.4 25–34y: 1.5 35–44y: 5.1 45–54y: 14.4 55–64y: 36.2 65–74y: 86.7 75–84y: 273.5 ≥85y: 883.3	Total: 51.3 1–4y: 0.3 5–14y: 0.2 15–24y: 0.3 25–34y: 1.1 35–44y: 3.8 45–54y: 10.2 55–64y: 24.7 65–74y: 67.4 75–84y: 255.1 ≥85y: 1,053.4	
		Deaths caused by influenza and pneumonia (J09–J18)	17.1 per 100,000 population*	Per 100,000 population: 1–4y: 0.7 5–14y: 0.3 15–24y: 0.4 25–34y: 0.9 35–44y: 1.9 45–54y: 4.8 55–64y: 12.0 65–74y: 29.6 75–84y: 93.8 ≥85y: 375.3	Per 100,000 population: Total: 16.6 1–4y: 0.8 5–14y: 0.2 15–24y: 0.5 25–34y: 0.9 35–44y: 2.1 45–54y: 5.1 55–64y: 14.0 65–74y: 34.5 75–84y: 110.1 ≥85y: 431.9	Per 100,000 population: Total: 17.6 1–4y: 0.5 5–14y: 0.3 15–24y: 0.4 25–34y: 0.9 35–44y: 1.7 45–54y: 4.4 55–64y: 10.2 65–74y: 25.3 75–84y: 81.3 ≥85y: 344.5	
CDC, 2018 [77] CDC's NVSS 2017	United States (50 states and District of Columbia)	Infant (<1 year) All causes of deaths	579.2 per 100,000 live births		632.0 per 100,000 live births	523.9 per 100,000 live births	
		Neonatal (<28 days) All causes of deaths	384.3 per 100,000 live births		418.6 per 100,000 live births	384.4 per 100,000 live births	
Virani, et al, 2020 [73] 2020 update of Heart Disease and Stroke Statistics, CDC Wide-	United States Death certificates data for sudden cardiac	SCD, any-mention in death certificates	97.1 per 100,000 population*	Per 100,000 population: <1y: 11.2			*Total rate is age-adjusted

ranging Online Data for Epidemiologic Research Database, (accessed June 7, 2018) 2017	death (SCD)			1–4y: 2.2 5–9y: 1.2 10–14y: 1.2 15–19y: 2 20–24y: 3.2 25–29y: 5.4 30–34y: 8 35–39y: 13.3 40–44y: 20.9 45–49y: 35.6 50–54y: 64.8 55–59y: 102.3 60–64y: 154.4 65–69y: 220.6 70–74y: 327.8 75–79y: 512.4 80–84y: 823.4			
							VACCINE PUBLICATIONS
Moro, et al, 2015 [78] Vaccine Adverse Event Reporting System (VAERS) July 1997–December 2013	United States Vaccinated individuals with any vaccine	2,149	2,149 per 2 billion doses of vaccines distributed (~1 per 1 million vaccine doses)	% of events: <1y: 54.2% 1–4y: 9.2% 5–9y: 1.4% 10–17y: 3.6% 18–45y: 6.5% 46–64y: 7.1% ≥65y: 17.5%	57%		Onset, in days: median (range): all reports, 3 (0–2,442); infants <1y, 2 (0–1,478)
McCarthy, et al, 2013 [79] Vaccine Safety Datalink (VSD) 2005–2008	United States Medically insured adults and children at 10 sites who received at least one vaccine	Deaths within 60d of vaccination 15,455	442.5 per 100,000 person-years*	Per 100,000 person-years: <1y: 103.05 1–4y: 17.65 5–10y: 7.28 11–24y: 19.34 25–64y: 279.19 65–74y: 1,089.25 75–84y: 2,819.19 ≥85y: 8,440.27	726.99 per 100,000 person-years	514.39 per 100,000 person-years	*Rate is age-adjusted

Table 16. Pregnancy loss, including spontaneous abortion (SAB)

Reference	Population	Total events	Rate		
			Total	By Maternal Age	
					NON-VACCINE PUBLICATIONS
American College of Obstetricians and Gynecologists, 2018 [80] *Practice bulletin of American College of Gynecology*	United States Early pregnancy loss defined as nonviable intrauterine pregnancy with either an empty gestational sac or sac containing an embryo or fetus without fetal heart activity within first 12 6/7 weeks of gestation		10% rate of EPL among clinically recognized pregnancies	20–30y: 9–17% 35y: 20% 40y: 40% 45y: 80%	Approximately 80% of all cases occur within first trimester
Ventura, et al, 2012 [81] CDC's National Vital Statistics Reports (NVSR) 1990-2008	United States 2008: 6.58 million pregnancies in women 15–44y of age Fetal loss	1.12 million	17.9 per 1,000 women		
American Society for Reproductive Medicine, 2012 [82] Practice committee opinion on treatment of recurrent pregnancy loss 2012	United States Pregnancy loss among recognized pregnancies		15–25% of recognized pregnancies		
Rossen, et al, 2018 [83] National Survey of Family Growth (NSFG) 1990–2011	United States Women 15–44y of age (N=20,012 women, 42,526 pregnancies) Self-reported pregnancy loss (miscarriage, stillbirth, ectopic pregnancy); EPL occurring <12w gestation		19.7% pregnancy loss rate (13.5% EPL rate)		Risk of pregnancy loss increased by 2% per year in unadjusted models and 1% per year in models adjusted for maternal age, race/Hispanic origin, socioeconomic factors, and other health-related factors
Lang and Nuevo-Chiquero, 2012 [84]	United States Nationally representative sample of		13–20% rate of miscarriage,		The increased incidence in reported miscarriages observed suggests

NSFG 1970–2000	non-institutionalized women 15–44y of age at time of interview; sample size varies by survey (administered in 1988, 1995, and 2002), totaling 26,940 women across the three cycles, of whom 10,959 had been pregnant at least once Miscarriage self-reported by women 13–25y of age		depending upon whether abortions are included or excluded from denominator		awareness of pregnancy (better and earlier testing) rather than lack of prenatal care
Avalos, et al, 2012 [85] *Literature review in MEDLINE 1967–2009*	United States Population-based studies in English language; life table methods used to calculate cumulative pregnancy loss rates by gestational week up to 20w		10-22% pregnancy loss rate*		*Weekly miscarriage rates available by included reference; overall, weekly miscarriage rate per 1,000 woman-weeks was highest prior to gestational week 12 and declined thereafter
Wilcox, et al, 1988 [86] Prospective observational study of preconception couples 1983–1985	United States Healthy women (N=221 women, 198 pregnancies) desiring pregnancy in several centers in Eastern US, evaluated with daily urine specimens for up to 6m for pregnancy detection and loss Clinically recognized losses were self-reported; clinically unrecognized losses were determined by urine hCG levels	43	31% pregnancy loss rate*		*Includes 22% incidence of clinically unrecognized early pregnancy loss

Table 17. Fetal deaths at ≥20w gestation

Reference	Population	Total events	Rate		Other measures
			Total	Race/Ethnicity	
NON-VACCINE PUBLICATIONS					
Hoyert and Gregory, 2020 [87] Cause-of-death Data from the Fetal Death File, CDC's NVSS 2015–2017	United States (34 states and the District of Columbia, in which less than 50% of deaths were attributed to Fetal death of unspecified cause; represents 60% of fetal deaths occurring in the US during this time period)	41,788	587.8 per 100,000 live births and fetal deaths	Number of fetal deaths by maternal race/ethnicity: Non-Hispanic White persons: 20,239 Non-Hispanic Black or African American persons: 10,835 Hispanic persons: 7,815	Number of deaths also available by cause of death, maternal age, sex of fetus, gestational age, birthweight, and plurality
	United States (entire)		594.8 per 100,000 live births and fetal deaths		
MacDorman and Gregory, 2015 [88] CDC's National Vital Statistics System (NVSS) 2013	United States (50 states, District of Columbia, American Samoa, Guam, the Northern Marianas, and Puerto Rico)	23,595	5.96 per 1,000 live births and fetal deaths	Maternal race/ethnicity, per 1,000 live births and fetal deaths: Non-Hispanic (NH) White persons: 4.88 NH Black or African American persons: 10.53 NH American Indian/Alaska Native persons: 6.22 NH Asian or Pacific Islander persons: 4.68 Hispanic: 5.22	Rates vary based on race/ethnicity, plurality, marital status, and gestational age at time of fetal death Rates available by maternal age, plurality, period of gestation, and by state

					Percentage of deaths available for marital status, sex of fetus, and birthweight
					VACCINE PUBLICATIONS
Panagiotakopoulos, et al, 2020 [89] Case-control study in Vaccine Safety Datalink (VSD) 2007–2015	United States Stillbirths (fetal loss ≥20w gestation) among women 14–49y		5.2 per 1,000 live births		Also, no association found between vaccination (with influenza or Tdap) during pregnancy and odds of stillbirth through case-control study of VSD data (2012–2015)

Table 18. Kawasaki's disease or syndrome (KD/KS)

Reference	Population	Total events	Rate					Other measures
			Total	By age group	Males	Females	Race/Ethnicity	
NON-VACCINE PUBLICATIONS								
CDC, 2020 [90] Population-based and hospitalization studies 2016	United States Children <18y of age Hospitalizations for KD	<18y: 5,440 <5y: 3,935	9-20 cases per 100,000 19.8 hospitalizations per 100,000 children <5y					
Chang, et al, 2019 [91] Review of discharge data from single medical center 2000–2015	United States New York, Buffalo Children <5y of age hospitalized at Women and Children's Hospital of Buffalo KD identified by ICD-9 and ICD-10 codes, classified as complete and incomplete KD	165	15.9 per 100,000 children <5y		13.1 complete KD cases per 100,000 children <5y (in Black or African American children: 14.2)	6.42 complete KD cases per 100,000 children <5y (in Black or African American children: 13.2)		Males/Females ratio: 1.68/1 Seasonality: predominance in winter

Holman and Christensen, et al, 2010 [92] Retrospective analysis of Hawaii State Inpatient Data 1996–2006	United States Hawaii Children <18y of age Hospitalization rate for KS diagnosed by ICD-9-CM code	528		Median age: 2y Per 100,000 children: <1y: 77.4 <5y: 50.4 <18y: 16.3	Per 100,000 children: <1y: 98.2 <5y: 55.2 <18y: 18.3	Per 100,000 children: <1y: 55.3 <5y: 45.3 <18y: 14.2	Per 100,000 children: Asian/Pacific Islander persons: 62.9 Japanese persons: 210.5 Native Hawaiian persons: 86.9 Chinese persons: 83.2 White persons: 13.7	
Ghimire, et al, 2019 [93] Hospital discharge data from National Kids' Inpatient Database (KID) 2009 and 2012	United States Children <18y of age (N=12,678,005 hospitalizations) KS cases identified by ICD-9-CM codes	10,486		Per 100,000 children: <5y: 18.5 <18y: 6.35			Asian or Pacific Islander persons/White persons ratio: 2.64/1	Males/Females ratio: 1.4/1.0 Rates were highest in January, highest in 0–4y age group
Holman and Belay, et al, 2010 [94] Retrospective analysis KID and Nationwide Inpatient Sample (NIS) 1997–2007	United States Children <18y of age Hospitalizations (in 2006) rate for KS diagnosed by ICD-9-CM code	5,523 (76.8% in children <5y)		Mean age: 3y Per 100,000 children: <5y: 20.8 <18: 7.5	24.2 per 100,000 children	16.8 per 100,000 children	Rate in Asian/Pacific Islander children: 30.3 per 100,000 children; highest of all racial groups	

McCrindle, et al, 2017 [95] Scientific statement for health professionals, American Heart Association (AHA)	World-wide Children <5y of age		Per 100,000 children: Japan (2012): 264.8 Hawaii, Japanese descent: 210.5 Hawaii, Caucasian descent: 13.7	<5y: 76%				Males/Females ratio: 1.6/1 Seasonal: cases peak in the winter and spring months in the United States
*****VACCINE PUBLICATIONS*****								
Hua, et al, 2009 [96] Vaccine Adverse Event Reporting System (VAERS) Mid-1990–October 2007	United States Children <5y of age Among adverse events passively reported to VAERS (N=239,535 reports)	97	Per 100,000 person-years*: RotaTeq, 1990–June 2007: 0.65 Pediarix, 1990–June 2007: 0.37 RotaTeq, June–October 2007: 2.78 Pediatrix, June–Oct 2007: 2.44	<5y: 91%	55.7%	40.2%		*Compared to US background incidence rate: 9–19 per 100,000 person-years for children <5y Time to onset: 91% within 30d, 35% 0–1d, 6% >30d (range 35–488d)

Abrams, et al, 2015 [97] Retrospective analysis of Vaccine Safety Datalink (VSD) 1996–2006	United States Children 0–6y of age at 7 managed care organization sites (N=1,721,186 children and 4,417,766 person-years) KD identified by ICD-9 codes, then classified as physician-diagnosed (PD) and verified cases 1–42d following vaccination	PD cases: 928 in 4,4417,766 person-years Verified cases: 151 in 1,816,363 person-years	Per 100,000 children per year: PD cases: 21.0 (vaccine exposed: 23.2; unexposed: 20.7) Verified cases: 8.3 (vaccine exposed: 5.1; unexposed: 8.8)		Per 100,000 children per year: PD cases: 24.3 Verified cases: 9.3	Per 100,000 children per year: PD cases: 17.5 Verified cases: 7.3		Rate ratio 1–42d post-vaccination: 0.89 (PD) and 0.50 (verified) Highest incidence in winter: 28.1 (PD) and 11.1 (verified) per 100,000 children per year Highest Incidence 1y old children: 34.1 (PD) per 100,000 children per year

Table 19. Multiple system inflammatory syndrome, in children (MIS-C)

Reference	Population	Total events	Rate				Other measures
			Total	By age group	Males	Females	
NON-VACCINE PUBLICATIONS							
CDC, 2020 [99] Multisystem Inflammatory Syndrome, health-department reported cases, available at: https://www.cdc.gov/mis-c/cases/index.html (Accessed December 4, 2020) Mid-May–October 20, 2020	United States Persons <21y of age Cases were reported in 44 states, New York City, and District of Columbia See site for updated case definitions	1,288			56%		*Population data not available for calculation of rates. Confirmed cases updated on CDC website as reported by health departments and additional cases are under investigation. 20 deaths were reported during the same period.
Dufort, et al, 2020 [100] New York State data March 1–May 10, 2020	New York Hospitalized patients <21y of age Laboratory-confirmed acute or recent severe respiratory syndrome SARS-CoV-2 infection, or if lacking laboratory confirmation, meets clinical and epidemiological criteria	99	2 per 100,000 persons <21y	0-5y: 31% 6-12y: 42% 13-20y: 26%	54%		During same period in New York, the incidence of laboratory-confirmed SARS-CoV-2 infection was 322 per 100,000 persons <21y of age

Table 20. Anaphylaxis

Reference	Population	Total events	Rate	Other measures			
			Total	By age group	Males	Females	
NON-VACCINE PUBLICATIONS							
Ma, et al, 2014 [101] National Inpatient Sample (NIS, 1999–2009); National Emergency Department Sample (NEDS, 2006–2009); Multiple Cause of Death Data (MCDD, 1999–2009)	United States NIS (N=8 million hospitalizations per year from ~1,000 hospitals in >45 states, ~20% stratified sample of US community hospitals) NEDS (N=25–30 million emergency department records from ~1,000 hospitals, ~20% stratified sample of US hospital emergency departments) Diagnosis of anaphylaxis: NIS via ICD-9-CM principal diagnosis code on discharge and NEDS via ICD-9-CM MCDD diagnoses via ICD-10 codes in death certificates	Hospitalizations (NIS): 5,681–7,708 per year (186–225 deaths) Emergency department visits without admission (NEDS): 17,735–21,822 per year (13–27 deaths) Hospitalizations and Emergency department visits without admission (NIS + NEDS): 25,329–29,530	Hospitalizations: 21.0–25.1 per million population Mortality: 0.63–0.76 per million population Emergency department visits: 58.8–71.1 per million population				Annual increase in number of hospitalizations of 2.23%, but a decrease in case fatality rate (CFR) of 2.35 CFR (NIS + NEDS): 0.25–0.33% (63–99 deaths per year)

			Hospitalizations and Emergency department visits without admission: 84.6–96.2 per million population				
Lee, et al, 2017 [102] Population-based incidence study from Rochester Epidemiology Project (REP) 2001–2010	United States, Minnesota, Olmsted County Diagnosess via ICD-9 codes and manual review using National Institutes of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network criteria for anaphylaxis	631	42.0 per 100,000 person-years*	Median age: 31y	Per 100,000 person-years: Overall: 43.8 0–9y: 42.0 10–19y: 55.9 20–29y:56.3 30–39y: 84.9 40–49y: 27.0 50–59y:28.4 ≥60y: 28.1	Per 100,000 person-years: Overall: 40.1 0–9y: 26.4 10–19y: 34.2 20–29y: 60.5 30–39y: 50.0 40–49y: 48.9 50–59y: 44.0 ≥60y: 24.5	*Age- and sex-adjusted incidence rate
Harduar-Morano, et al, 2011 [103] Review of Florida Emergency Department records 2005–2006	United States Florida (N=36,459,197) Emergency Department visits Diagnoses via ICD-9-CM and a validated ICD-9-CM–based	2,751			(n=1,173) Per 100,000 Floridians: Overall: 6.6 0–4y: 8.2 5–14 y: 5.9	(n=1,578) Per 100,000 Floridians: Overall: 8.7 0–4y: 6.2 5–14y: 5.3	

	algorithm				15–24y: 6.2 25–34y: 6.7 35–44y: 7.6 45–54y: 6.6 55–64y: 6.8 65–74y: 6.7 75–84y: 5.0 ≥85y: 3.2	15–24y: 10.4 25–34y: 10.9 35–44y: 9.9 45–54y: 10.7 55–64y: 7.8 65–74y: 8.0 75–84y: 4.7 ≥85y: 4.0	
Fuzak and Trainor, 2013 [104] Retrospective review of hospital records 1986–1990 and 2002–2006	United States Illinois, Chicago Patients <18y of age at single hospital (both inpatient and emergency department visits) Diagnosis: 2 systemic symptoms or 1 systemic symptom plus 1 cutaneous symptom	1986–1990: 53 2002–2006: 117	1986–1990: 30.5 per 100,000 Emergency department visits 2002–2006: 38 per 100,000 Emergency department visits	Median age (range): 1986–1990: 6.9y (6m–16.2y) 2002–2006: 7.2y (4m–17.7y)			Etiology: food allergens most common (43%) 80% presented in Emergency department
VACCINE PUBLICATIONS							
McNeil, et al, 2016 [105] Retrospective analysis from 9 Vaccine Safety Datalink (VSD) sites 2009–2011	United States (N=2.1 million children and 7.2 million adults; 17,606,500 vaccine visits and 25,173,965 vaccine doses)	33	Overall: 1.31 per 1 million doses Trivalen	Per 1 million doses: 0–17y: 1.45 18–49y: 1.78 ≥50y: 0.78	1.14 per 1 million doses	1.45 per 1 million doses	No variation by age Onset 0–20h after vaccination

	Vaccine-associated cases of anaphylaxis via Brighton Collaboration case definition and ICD-9-CM codes		t influenza vaccine: 1.32 per 1 million doses				
Oberle, et al, 2016 [106] Retrospective review of reports to German surveillance unit for rare pediatric diseases 2008–2010	Germany; children and adolescents <18 years with suspected anaphylaxis <48h after immunization (928,500 doses of AS03 adjuvanted A/H1N1 pandemic influenza vaccine)	All vaccine cases: 22 AS03 adjuvanted A/H1N1 cases: 8	Range for specific vaccines: 0.4–127.6 cases per 1 million doses AS03 adjuvanted A/H1N1: 11.8 (95% CI: 9.1–28.2) cases per 1 million doses				AS03 adjuvanted A/H1N1 pandemic influenza vaccine associated with a higher risk of anaphylaxis when compared with other vaccines

Table 21. Idiopathic or immune thrombocytopenic purpura (ITP)

Reference	Population	Total events	Rate				Other measures
			Total	By age group	Males	Females	
NON-VACCINE PUBLICATIONS							
Weycker, et al, 2020 [107] Retrospective cohort of two large integrated US private healthcare claims databases Marketscan and PharMetrics Plus 2010-2016	United States N=~120 million persons with private insurance Patients with evidence of ITP identified based on ≥1 hospitalization with a diagnosis code for ITP or ≥2 ambulatory (nonlab) encounters with a diagnosis code for ITP separated by ≥30 days	11,028	6.1 per 100,000 persons per year*	Per 100,000 persons per year: 0-4y: 8.1 5-17y: 3.6 18-49y: 4.3 50-64y: 5.9 ≥65: 13.7	5.5 per 100,000 persons per year	6.7 per 100,000 persons per year	*age and sex adjusted incidence rate Annual ITP incidence rates were roughly comparable across calendar years (i.e. 2012–2015)
Shaw, et al, 2020 [108] Retrospective cohort of MarketScan® Commercial Claims an Encounters Database 2011–2016	United States Children <18y of age (N=48,003,679 person-years, male 24,520,702 person-years and female 23,482,978 person-years) ITP via ICD-9 or ICD-10 codes	4,214	8.8 per 100,000 person-years	Per 100,000 person-years: <2y: 14.8 2–4y: 12.1 5–9y: 7.1 10–14y: 6.7 15–17y: 7.7	9.0 per 100,000 person-years	8.6 per 100,000 person-years	
Glanz, et al, 2008 [109] Retrospective cohort study of 8 managed care organizations in the Vaccine Safety Datalink (VSD) 1991–2000	United States 8 managed care organization VSD sites Children aged <18y of age (1 site only included children 12–23m of age) (N=5.5	259*	2.7 per 100,000 person-years	Mean age: 6.23y	50%	50%	*Of the 259 cases of ITP, 197 (76%) were acute and 60 (23%) were chronic; 1 serious hemorrhagic outcome (0.39%)

	million children in this VSD cohort) ITP diagnoses via ICD-9 and chart review						Authors note that incidence rate is at lower end of published range for ITP; this may be because of exclusion of mild cases
Watts, 2004 [110] Retrospective chart review hospital and clinic records at Children's Hospital of Alabama 1993–2003	United States Alabama, Birmingham Children <18y of age treated at referral hospital (estimated from state population of 1,100,000 children) ITP discharge diagnoses via ICD codes	409	4 per 100,000 children per year	Median age: 5y	49%	51%	No deaths
							*****VACCINE PUBLICATIONS*****
O'Leary, et al, 2012 [111] Retrospective cohort study of 5 managed care organizations 2000–2009	United States Children 6w–17y of age receiving care in one of 5 Kaiser Permanente healthcare systems (N=1.8 million children who received ≥1 vaccine) ITP diagnosis: ICD-9 codes followed by chart review for platelet count ≤50,000/μL with normal red and white blood cell indices, the presence of clinical signs and symptoms of spontaneous bleeding,	197	1.9 per 100,000 doses of MMR				No deaths; 1 case of after vaccine-associated ITP required transfusion Study provides incident rate ratios (IRR) for risk of ITP during 1–42 days after vaccination vs. control periods; elevated IRR ($p<0.05$) by vaccine and age group: MMR, 12–19m, 5.48; Hepatitis A, 7–17y, 23.14;

	and the absence of fever						Varicella, 11–17y, 12.14; Tdap 11–17y, 20.29; Note: the authors state these IRRs are hypothesis-generating, except for MMR with a known association to ITP
France, et al, 2008 [112] Retrospective cohort from 8 VSD sites 1991–2000	United States Children aged <18y of age (1 site only included children 12–23m of age) 1,036,689 children received 1,107,814 doses of MMR vaccine ITP diagnosis: ICD-9 codes and platelet count of ≤50,000/μL with normal red and white blood cell indices, the presence of clinical signs and symptoms of spontaneous bleeding, and the absence of fever. A case was excluded if in the 6w before diagnosis the child was exposed to platelet-depleting medications	259	1 per 40,000 doses of MMR in children 12–23m and 12–15m of age				No deaths due to ITP Conclusion of authors: though MMR was associated with increased risk of ITP, the attributable risk is low
Klein, et al, 2015 [113] Retrospective cohort	United States Children 12–23m of age	MMRV: ITP1: 7	Per 100,000 doses:				Conclusion: study detected no

from 8 VSD sites 2000–2012	Estimate risk of ITP in 1–42d following vaccination with: MMRV doses: 123,200 MMR+V doses: 584, 987 Definition ITP1 (strict): 2 platelet counts of ≤50,000/µL within 7d of each other and Definition ITP2 (relaxed): 2 platelet counts of ≤150,000/µL within 7d of each other	ITP2: 10 MMR+V: ITP1: 33 ITP2: 70	MMRV: ITP1: 5.89 ITP2: 8.41 MMR+V: ITP1: 5.73 ITP2: 12.16				difference in risk between recipients of MMRV compared with MMR+V; the study also presented ITP cases per 100,000 doses in the 14–28d after vaccination (data not shown)