Safety of Quadrivalent Meningococcal Polysaccharide Diphtheria Toxoid-Conjugate Vaccine in Adolescents

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BACKGROUND

- Quadrivalent meningococcal conjugate (MenACWY-D) vaccine recommended for routine use in adolescents in 2005
- After case reports of Guillain-Barré syndrome (GBS) following MenACWY-D[1], meta-analysis concluded that attributable risk of GBS after MenACWY-D was unlikely to exceed 1 case per million vaccinations[2]; a recent post-marketing study found no new safety concerns related to MenACWY-D[3]
- We conducted a retrospective cohort study to assess risk of 10 outcomes, including GBS, using data from the Vaccine Safety Datalink[4]

METHODS

- Population: 11-18 year olds receiving MenACWY-D in 2005-2014
- Enrollment history of ≥12 months prior to vaccination at one of six participating health care organizations
- Pre-specified outcomes identified using International Classification of Diseases, Ninth Revision (Table 1)
- Self-controlled risk interval design to estimate relative risk, with control window equal to five times the risk window

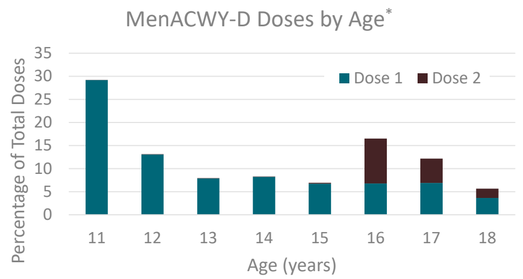
Table 1. Algorithms for identifying outcomes

Outcome	Code restrictions	Setting*	Risk Window (days)
Acute disseminated encephalomyelitis**	1st in 365 days	InP, ED	1-42
Acute transverse myelitis**	1st ever	InP, ED	1-42
Anaphylaxis**	1st in 2 days	InP, OutP, ED	0-2
Bell's palsy	1st in 365 days	OutP, ED	1-28
Chronic inflammatory demyelinating polyneuropathy**	1st in 42 days	InP, OutP, ED	1-56
Fever	1st in 7 days	InP, OutP, ED	1-6
GBS**	1st in 42 days	InP, OutP, ED	1-42
Henoch-Schönlein purpura**	1st ever	InP, OutP, ED	1-42
Seizure	1st ever	InP, ED	0-7
Syncope	1st in 2 days	InP, ED	0

*InP=inpatient, OutP=outpatient, ED=emergency department
**Confirmed by medical record review

RESULTS

- 1,403,356 doses of MenACWY-D provided to study population
- Study population was 50% male, 50% female
- 17.5% of the doses in the study were 2nd dose of MenACWY-D
- Vaccination patterns reflect adolescent vaccine recommendations



*percentages for doses 3 and 4 were <0.2% combined across 11-18 year olds

Table 2. Number of cases and results of self-controlled risk interval analysis

Outcome	# Cases Risk Window	# Cases Control Window	Relative Risk	95% Confidence Interval
Acute disseminated encephalomyelitis	0	2	NE*	NE
Acute transverse myelitis	0	3	NE	NE
Anaphylaxis	3	8	1.88	0.50-7.07
Bell's palsy	43	198	1.09	0.78-1.51
Chronic inflammatory demyelinating polyneuropathy	0	0	NE	NE
Fever	387	1306	1.48	**1.32-1.66**
GBS	3	6	2.50	0.62-9.99
Henoch-Schönlein purpura	9	29	1.55	0.73-3.28
Seizure	20	87	1.15	0.71-1.87
Syncope	66	57	5.79	**4.06-8.25**

*NE – not estimated, no observed events in risk window

Table 3. Comparison with previous studies of GBS following MenACWY-D

Study Lead Author	Number of Menactra Doses	Number of GBS Cases	Cumulative Incidence		Attributable Risk	
			GBS cases per million doses	One-sided 95% CI upper bound	GBS cases per million doses	One-sided 95% CI upper bound
Velentgas[5]	1,431,906	0	0	2.09	0	1.46
Yih[2]	889,684	0	0	3.37	0	2.74
Combined from above[2]	2,321,590	0	0	1.29	0	0.66
Myers (this study)	1,403,356	3	2.14	5.53	1.51	4.90

- Elevated relative risks were detected for fever and syncope following vaccination with MenACWY-D (Table 2)
- No cases of acute disseminated encephalomyelitis, acute transverse myelitis, or chronic inflammatory demyelinating polyneuropathy were detected in the post-immunization risk period; few cases of other outcomes led to relatively unstable relative risk estimates (Table 2)
- The risk of GBS, if any, is small after MenACWY-D; the upper bound of the 95% CI suggests <5 excess cases of GBS per million vaccinations (Table 3)

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CONCLUSIONS

- Risk of fever was modestly increased after MenACWY-D
- Risk of syncope was increased after MenACWY-D - providers should continue to follow recommended procedures to prevent falling injuries after vaccination
- Risks of seizure or Bell's palsy were not increased after MenACWY-D
- Our study is consistent with previous findings that the risk of GBS after MenACWY, if any, is small

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