

Meningococcal Carriage Evaluation in Response to a Serogroup B Meningococcal Disease Outbreak and Mass Vaccination Campaign at a College — Rhode Island, 2015-2016

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Background

Meningococcal Disease & Vaccines

- Meningococcal disease, caused by the bacterium *Neisseria meningitidis* (*Nm*), is a serious illness with a 10-15% case-fatality ratio.
- Serogroups B, C, and Y are the most common in the U.S.
- The meningococcal conjugate vaccine protects against serogroups A, C, W, and Y.

Meningococcal Transmission

- Nm* is carried in the nasopharynx, and most people who acquire *Nm* remain completely asymptomatic.
- <1% of exposed persons develop invasive disease.
- The bacteria are spread through close contact, specifically via respiratory or oral secretions from patients or asymptomatic carriers.
- Important risk factors for meningococcal disease and carriage among adolescents and young adults include age,^{1,2} social mixing,³ and smoking.¹

Serogroup B Disease & Vaccines

- The meningococcal conjugate vaccine routinely administered to all adolescents does not protect against serogroup B, leaving persons aged 16 to 21 years at risk for serogroup B meningococcal disease.
- Serogroup B meningococcal disease caused 8 US university outbreaks from 2009-2016, including one involving 2 cases at a Rhode Island college in February 2015 (sequence type ST-9069).
- MenB-FHbp (Trumenba®, Pfizer), a recently licensed serogroup B meningococcal (MenB) vaccine, was used in response to this outbreak in Rhode Island.

- The three doses were provided in Feb, April, and Sept 2015, with vaccination coverage of 94% with dose 1, 80% with dose 2, and 77% with dose 3.
- Incoming freshmen in Fall 2015 were also offered to begin the series.

Meningococcal Vaccine Impact on Meningococcal Carriage

- MenC vaccines: Reduced serogroup C carriage in UK by 66%⁴
- MenA (PsA-TT) vaccine: Reduced serogroup A carriage by ≥98%^{5,6}
- Our understanding of MenB vaccine impact on carriage is limited:
 - MenB-4C (Bexsero®, GlaxoSmithKline): 18% (95% CI: 3-31%) reduction in carriage of any meningococcal bacteria, no effect on serogroup B carriage⁷
 - No data regarding MenB-FHbp impact on carriage has been published.

Objectives

- In February 2015, Rhode Island Department of Health declared a meningococcal disease outbreak.⁸ To better understand meningococcal carriage in an outbreak setting, this evaluation aimed to:
 - Determine meningococcal carriage prevalence among students in an outbreak setting
 - Assess MenB-FHbp vaccination impact on carriage

Methods

- 4 carriage evaluations during the year post-outbreak, each consisting of a short questionnaire assessing risk factors for meningococcal carriage and disease, an oropharyngeal swab, and specimen evaluation via bacterial culture, slide agglutination, real-time PCR, and whole genome sequencing.
- All undergraduate students at the college and graduate students who lived on campus were eligible to participate.
- General estimating equation methods for repeat measures using Poisson regression were used to calculate prevalence ratios.

Table 1. Carriage evaluation timing

Carriage evaluation round	Date	Timing
1	February 2015	Baseline/Dose 1
2	April 2015	Dose 2
3	September 2015	Upperclassmen: Dose 3, Freshmen: Dose 1
4	March 2016	One year post outbreak, Freshmen: Dose 3

Results

Table 2. MenB mass vaccination campaign coverage, carriage evaluation participants, and results

Round	Carriage evaluation participants	<i>N. meningitidis</i> carriage, N (%)	Serogroup B by rt-PCR, N (%)	Serogroup B by SASG ^a , N (%)	Outbreak strain detected ^b
1	717	175 (24)	31 (4)	9 (1.3)	No
2	878	211 (24)	36 (4)	12 (1.4)	Yes – 1 carrier
3	622	123 (20)	26 (4)	7 (1.1)	Yes – 1 carrier
4	626	130 (21)	22 (4)	6 (1.0)	No

^aAll isolates that were serogroup B by slide agglutination serotyping (SASG) were also serogroup B by real-time PCR; ^bThe outbreak strain was carried by the same individual in rounds 2 and 3

Figure 1. Distribution of meningococcal carriage isolate serogroups by real-time PCR

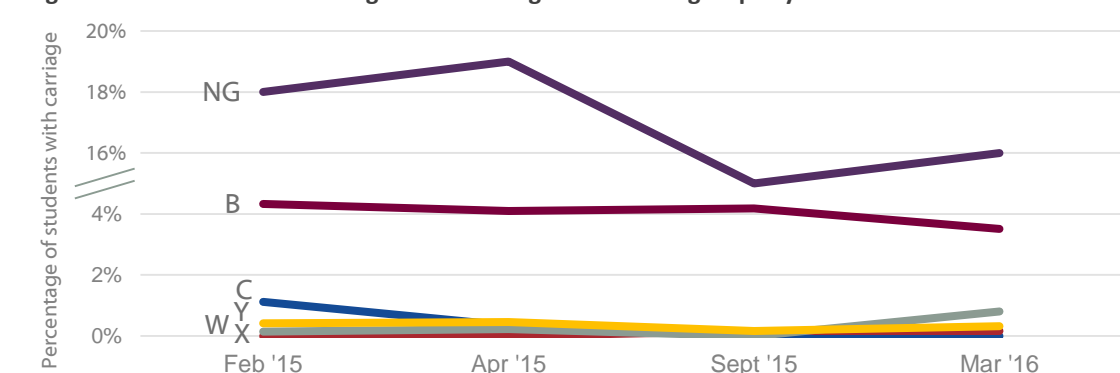


Table 3. Within-individual changes in carriage over time

Received MenB-FHbp vaccine doses ^a	Lost carriage		Acquired carriage	
	Any meningococci	Serogroup B by rt-PCR	Any meningococci	Serogroup B by rt-PCR
1	13	2	20	3
2	32	8	16	4
3	5	1	9	3
Total	50	11	45	10

^aRefers to vaccine doses received ≥2 weeks prior to the latter date of specimen collection

Table 4. Participant characteristics and multivariable associations with meningococcal carriage

Characteristic	Total N ^a (N=2,843)	<i>N. meningitidis</i> carriage, N (%)	Prevalence Ratio ^b (95% CI)	p-value
Round 1	717	175 (24)	1.0	
Round 2	878	211 (24)	0.7 (0.4, 1.1)	0.111
Round 3	622	123 (20)	0.6 (0.4, 0.9)*	0.013
Round 4	626	130 (21)	0.6 (0.4, 1.0)	0.062
Graduation Year				
2019	372	70 (19)	1.1 (0.8, 1.7)	0.503
2018	734	137 (19)	1.0	
2017	764	224 (29)	1.5 (1.2, 1.9)*	<0.001
2016	614	144 (23)	1.2 (1.0, 1.5)	0.107
2015	342	62 (18)	0.9 (0.7, 1.2)	0.608
Graduate student	17	2 (12)	0.8 (0.2, 4.1)	0.837
Male	1,093	313 (29)	1.3 (1.1, 1.5)*	<0.001
Recent antibiotic use ^c	312	30 (10)	0.4 (0.3, 0.5)*	<0.001
Smoking ^c	741	238 (32)	1.3 (1.1, 1.5)*	0.003
Visit bars, clubs, or parties ≥1x/wk	1,987	540 (27)	1.8 (1.5, 2.1)*	<0.001
Received MenB-FHbp vaccine doses ^d				
0	874	196 (22)	1.0	
1	961	233 (24)	1.5 (1.0, 2.4)	0.074
2	839	176 (21)	1.4 (1.0, 2.1)	0.082
3	169	34 (20)	1.6 (0.9, 2.7)	0.124

^aParticipants can have participated in multiple rounds; ^bPrevalence ratios account for repeat participants using GEE methods and have been adjusted for second-hand smoking; ^cIn the past 30 days; ^dRefers to vaccine doses received ≥2 weeks prior to date of specimen collection; *Statistically significant at the alpha = 0.05 level

Conclusions

- In each round, 20-24% of students carried meningococcal bacteria, and 4% carried serogroup B by real-time PCR.
 - This overall carriage prevalence is comparable to prevalences of ≤34% among UK university students.⁷
 - However, it was higher than recent U.S. estimates of 1-8% among the general population.^{9,10}
- Only 1 carrier of the outbreak strain was identified; no further serogroup B cases associated with the college have occurred.
- We did not find evidence that MenB-FHbp vaccination impacts carriage, at either the population or individual level.
- These results inform U.S. MenB vaccine guidelines, both for use in adolescents and young adults, and specifically in outbreak settings.
- If MenB vaccines do not affect carriage, this reinforces the need for high vaccination coverage during outbreaks to protect each individual and emphasizes the role of chemoprophylaxis for close contacts.
- Whole genome sequencing is underway to further characterize the isolates.
- Will compare findings with carriage evaluations conducted at 2 other universities (see poster 722).

References

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