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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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Abstract

Background—Serogroup B meningococcal disease caused 7 US university outbreaks during 2013–2016. *Neisseria meningitidis* can be transmitted via asymptomatic nasopharyngeal carriage. MenB-FHbp (factor H binding protein), a serogroup B meningococcal (MenB) vaccine, was used to control a college outbreak. We investigated MenB-FHbp impact on meningococcal carriage.

Methods—Four cross-sectional surveys were conducted in conjunction with MenB-FHbp vaccination campaigns. Questionnaires and oropharyngeal swabs were collected from students. Specimens were evaluated using culture, slide agglutination, real-time polymerase chain reaction (rt-PCR), and whole genome sequencing. Adjusted prevalence ratios (aPRs) were calculated using generalized estimating equations.

Results—During each survey, 20%–24% of participants carried any meningococcal bacteria and 4% carried serogroup B by rt-PCR. The outbreak strain (ST-9069) was not detected during the initial survey; 1 student carried ST-9069 in the second and third surveys. No carriage reduction was observed over time or with more MenB-FHbp doses. In total, 615 students participated in

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Author contributions. H. M. S., M. W., J. R. M., S. W. M., L. A. M., X. W., and M. P. conceived and designed the study and wrote the study protocol. H. M. S., N. A. S., K. S., U. B., and M. P. wrote the ethics submissions. N. A. S., K. V. K., K. S., C. V., and U. B. provided administrative and logistical support and recruited volunteer staff. H. M. S., M. W., L. A. M., J. V., and M. P. trained and supervised staff in consent collection, specimen collection, and transport procedures. H. M. S. and M. W. were responsible for data collection and data storage. M. W., J. V., and X. W. did the laboratory analysis. H. M. S. reviewed vaccination records. H. M. S., J. R. M., S. W. M., L. A. M., and M. P. developed the data analysis plan. H. M. S. did the data analysis. H. M. S., M. W., J. R. M., L. A. M., and M. P. drafted the manuscript. All authors reviewed and contributed to the final manuscript. All other members of the Rhode Island Meningococcal Carriage Evaluation Team provided invaluable assistance.

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multiple surveys: 71% remained noncarriers, 8% cleared carriage, 15% remained carriers, and 7% acquired carriage. Ten students acquired serogroup B carriage: 3 after 1 MenB-FHbp dose, 4 after 2 doses, and 3 after 3 doses. Smoking (aPR, 1.3; 95% confidence interval [CI], 1.1–1.5) and male sex (aPR, 1.3; 95% CI, 1.1–1.5) were associated with increased meningococcal carriage.

Conclusions—Carriage prevalence on campus remained stable, suggesting MenB-FHbp does not rapidly reduce meningococcal carriage or prevent serogroup B carriage acquisition. This reinforces the need for high vaccination coverage to protect vaccinated individuals and chemoprophylaxis for close contacts during outbreaks.

Keywords

meningococcal disease; serogroup B; vaccines; nasopharyngeal carriage; outbreak

Meningococcal disease, caused by *Neisseria meningitidis*, is a rare but severe infection that can unexpectedly strike otherwise healthy persons. In the United States, serogroup B accounts for approximately half of meningococcal disease cases among persons aged 17–22 years and it caused 7 university-based outbreaks during 2013–2016 [1–4].

The human nasopharynx is the primary reservoir for *N. meningitidis* [5], which is transmitted via large-droplet respiratory tract secretions from persons with asymptomatic nasopharyngeal carriage or meningococcal disease [6]. As the majority of transmission is due to asymptomatic carriers, decreasing carriage provides herd protection against meningococcal disease. Carriage prevalence varies widely by setting and is age related, peaking during late adolescence [5, 7]. Carriage duration varies by serogroup and strain, as well as host and environmental factors, but often persists for weeks to months [8]. Risk factors for both meningococcal disease and carriage among adolescents and young adults include age [9, 10], social mixing [11], and smoking [9].

Meningococcal vaccines that target serogroups A, C, W, and Y capsular polysaccharides have been used globally since the 1970s. However, serogroup B vaccine development has been challenging due to poor immunogenicity resulting from antigenic similarity between human neural cells and the serogroup B capsular polysaccharide and concerns about potential autoimmunity [12]. In 2014–2015, 2 serogroup B meningococcal (MenB) vaccines, MenB-FHbp (factor H binding protein; Trumenba, Pfizer) [13] and MenB-4C (Bexsero, GlaxoSmithKline) [14], were licensed in the United States for persons aged 10–25 years. Both MenB vaccines contain outer membrane proteins that can be found in many meningococcal strains. MenB-FHbp induces immune responses to FHbp and includes a variant from each FHbp subfamily (A and B) [13]. MenB-4C contains 3 recombinant proteins (neisserial adhesion A, FHbp fusion protein [subfamily B], and neisserial heparin-binding antigen fusion protein) in addition to outer membrane vesicles that contain outer membrane protein PorA [14]. Due to genetic heterogeneity and variability in phenotypic expression of these outer membrane proteins, MenB vaccines are not expected to protect against all serogroup B strains [15]. Conversely, some cross-protection may be provided against nonserogroup B strains that express 1 or more of the vaccine antigens [16].

Although MenB vaccines are not routinely recommended for all adolescents, the Advisory Committee on Immunization Practices recommends their use in persons aged 10 years at increased risk for serogroup B meningococcal disease, including during outbreaks [17]. While MenB vaccines are immunogenic against serogroup B and therefore likely help protect vaccinated individuals against disease, our understanding of MenB vaccine impact on meningococcal carriage is limited [15]. To date, no data have been published regarding MenB-FHbp effect on carriage. However, vaccine impact on carriage is an important consideration for use of meningococcal vaccines.

On 29 January 2015 and 5 February 2015, 2 cases of serogroup B meningococcal disease occurred in undergraduate students (1 freshman and 1 sophomore) at Providence College [4], a college with approximately 4500 students in Providence, Rhode Island. Both cases were caused by a rare strain of serogroup B sequence type (ST)-9069, not previously seen in the United States but identified in 1 carriage isolate from Ireland in 2009 [18]. Both isolates were serogroup B by slide agglutination, real-time polymerase chain reaction (rt-PCR), and whole genome sequencing. Neither case was fatal. Molecular testing on the outbreak strain detected the gene coding for FHbp B24 [19], suggesting that either MenB vaccine licensed in the United States may help provide protection against the outbreak strain. In response to the outbreak, 71 contacts received ciprofloxacin chemoprophylaxis, and a mass vaccination campaign using MenB-FHbp was implemented. In conjunction, we conducted a meningococcal carriage evaluation to assess carriage prevalence and the impact of MenB-FHbp vaccination on carriage.

METHODS

MenB-FHbp Vaccination

During this outbreak, MenB-FHbp was recommended as a 3-dose schedule administered at 0, 2, and 6 months. At Providence College, MenB-FHbp was offered to eligible persons through 5 mass vaccination campaigns held in February, April, September, and November 2015 and March 2016. Eligible persons included all undergraduate students, graduate students or staff aged <25 years who lived or worked on campus, persons in an intimate physical relationship with an undergraduate, and asplenic persons or persons with an immunocompromising condition known to place them at increased risk for meningococcal disease [17]. Incoming freshman in the academic year following the outbreak were also offered MenB-FHbp. Persons who declined vaccination were required to sign opt-out forms.

Meningococcal Carriage Evaluation

Four cross-sectional carriage evaluation rounds were conducted in conjunction with MenB-FHbp vaccination clinics in February, April, and September 2015 and March 2016 (Table 1). The first 3 rounds coincided with administration of the 3 doses of MenB-FHbp for students attending Providence College at the time of the outbreak, while the fourth round examined MenB-FHbp impact 1 year post-outbreak and coincided with administration of the third dose for incoming freshmen and other students needing to complete the MenB-FHbp series. All undergraduate students at Providence College and graduate students who lived on campus were eligible to participate regardless of MenB-FHbp vaccination status. After

obtaining informed consent, participants self-administered a short questionnaire that assessed risk factors for meningococcal disease and carriage, and an oropharyngeal swab was collected from each participant. Swabs were collected by staff from the Centers for Disease Control and Prevention (CDC) and the Rhode Island Department of Health and volunteer medical students and residents, who were trained to use a standardized technique. Meningococcal vaccination records for each participant, including the number of doses and dates of previous quadrivalent meningococcal conjugate (MenACWY) or MenB vaccination, were abstracted from student health records. Only documented doses received at least 2 weeks prior to specimen collection were included. Students could participate in multiple rounds of the evaluation. Due to the 3-month lag between specimen collection and sequence results, students found to be carrying *N. meningitidis* were not offered antibiotics to eliminate carriage. This evaluation was considered public health practice and did not require CDC Institutional Review Board review.

Laboratory Methods

Oropharyngeal swabs were immediately used to inoculate a modified Thayer-Martin (MTM) agar plate (BD BBL, Franklin Lakes, New Jersey). MTM plates were incubated at 37°C and checked for growth of *N. meningitidis* at 24, 48, and 72 hours. Colonies with typical *Neisseria* morphology were subcultured onto a blood agar plate (BD BBL), and Gram staining (BD BBL), oxidase testing (Hardy Diagnostics, Santa Maria, California), *sodC* rt-PCR, and API *Neisseria-Haemophilus* strip testing (bioMerieux, Durham, North Carolina) were used to determine bacterial identity [20]. *Neisseria meningitidis* isolates were further characterized using rt-PCR serogrouping and slide agglutination [20]. rt-PCR targeting meningococcal genes in the *cap* locus of *N. meningitidis* isolates could detect serogroups A, B, C, W, X, and Y. Slide agglutination detected expression of the capsular polysaccharide, with antiserum (DIFCO; BD BBL) available to detect serogroups A, B, C, E, W, X, Y, and Z. Any *N. meningitidis* that were not identified as one of the assessed serogroups by rt-PCR and slide agglutination were considered nongroupable according to that method.

Serogroup B meningococcal isolates were further characterized with whole genome sequencing to confirm whether the outbreak strain (ST-9069) remained in circulation. Genomic DNA of these isolates was extracted and prepared for sequencing with the ArchivePure DNA purification kit (5 Prime, Gaithersburg, Maryland), Ampure (Beckman Coulter Inc., Indianapolis, Indiana), and dual-index NEBNext Ultra sequencing libraries (New England Biolabs Inc., Ipswich, Massachusetts). Sequencing was performed on the Illumina MiSeq using MiSeq 250 × 250 cycle paired-end sequencing kits (Illumina, San Diego, California). Raw sequence reads were reviewed for read quality and trimmed as previously described [21]. Quality-trimmed reads were then assembled as paired reads into contigs using CLC Bio Genomics Workbench (v8.5.1, Qiagen, Waltham, Massachusetts). Once assembled, multilocus sequence typing alleles were identified through a Basic Local Alignment Search Tool (BLAST) search against www.PubMLST.org/neisseria alleles [18, 22]; combination of alleles resulted in a sequence type.

Statistical Methods

Questionnaires were checked for completeness to prevent missing data. Bivariate and multivariable prevalence ratios (PRs) and 95% confidence intervals (CIs) for associations with meningococcal carriage were estimated using generalized estimating equations for repeated measures using modified Poisson regression with an unstructured correlation matrix. Among students who participated in multiple carriage evaluation rounds, within-individual changes in carriage over time were examined. SAS 9.3 (Cary, North Carolina) was used for analyses.

RESULTS

Vaccination Campaign

Among eligible persons, 94% (3525/3745) received the first dose of MenB-FHbp, 80% (2988/3741) the second, and 75% (3045/4087) the third.

Participant Characteristics

In total, 2843 oropharyngeal swabs were collected from 2014 unique individuals, with 622 to 878 participants in each of the 4 carriage rounds (Table 1). As the evaluation spanned 2 academic school years, the class of 2019 was only included in rounds 3 and 4 and accounted for 51% of round 4 participants (Table 1). The proportion of participants who lived on campus ranged from 73% to 91% per round; 38% were male. A high proportion of students smoked or had second-hand smoke exposure: 26% and 46%, respectively; 23% of students reported both smoking and second-hand smoke exposure. Social mixing was common, as 67%–74% of students reported visiting bars, clubs, or parties 1 time per week.

Overall, 95% of participants received MenACWY at least 2 weeks prior to specimen collection, generally received prior to college entry (Table 1). In round 1, no students had received MenB-FHbp more than 2 weeks prior to oropharyngeal swab collection. In round 2, 99% had received 1 dose of MenB-FHbp. In round 3, 81% had received 2 doses, and in round 4, 54% had received 2 doses and 27% had received the full 3-dose series.

Overall Meningococcal Carriage

In round 1, conducted 11–15 days following the second case in the outbreak, 24% of participants were carrying *N. meningitidis* (Table 2). This proportion remained fairly stable over the next year, with 24% carriage in round 2, 20% carriage in round 3, and 21% carriage in round 4. In round 3, during the first week of the following academic school year, meningococcal carriage prevalence was 16% among incoming freshmen and 19%–21% among returning upperclassmen.

Serogroup-Specific Carriage

By rt-PCR, 4% of participants carried serogroup B *N. meningitidis* in each of the 4 rounds (Table 2). By slide agglutination, 1.0%–1.4% of participants carried bacteria that expressed the serogroup B capsule, all of which were also serogroup B by rt-PCR. In total, less than 2% of participants carried serogroups C, E, W, X, Y, or Z by either rt-PCR or slide

agglutination; 17% carried nongroupable *N. meningitidis* by rt-PCR; and 20% carried nongroupable bacteria by slide agglutination.

Associations With Carriage

Compared with round 1, round 3 was associated with slightly decreased meningococcal carriage in both bivariate and multivariable models (Table 3). The class of 2017, who were sophomores at the time the cases occurred, had the highest carriage prevalence (adjusted prevalence ratio [aPR], 1.5; 95% CI, 1.2–1.9 compared to the class of 2018). Male sex (aPR, 1.3; 95% CI, 1.1–1.5), smoking (aPR, 1.3; 95% CI, 1.1–1.5), and visiting bars, clubs, or parties at least once per week (aPR, 1.8; 95% CI, 1.5–2.1) were associated with increased carriage, while recent antibiotic use (aPR, 0.4; 95% CI, 0.3–0.6) was associated with decreased carriage. In bivariate analysis, documented receipt of MenB-FHbp vaccine doses was associated with increased meningococcal carriage, likely due to increasing opportunity to be both vaccinated and colonized with increased time on campus (Table 3). In multivariable models, MenACWY vaccine or MenB-FHbp vaccine doses were not associated with any meningococcal carriage (Table 3) or serogroup B carriage by rt-PCR (Table 4). Similar to associations with any meningococcal carriage, male sex (aPR, 1.6; 95% CI, 1.0–2.4), smoking (aPR, 1.5; 95% CI, 1.0–2.2), and visiting bars, clubs, or parties at least once per week (aPR, 1.5; 95% CI, 1.0–2.3) were associated with increased serogroup B carriage by rt-PCR, while those reporting recent antibiotic use (aPR, 0.4; 95% CI, 0.2–0.9) had decreased serogroup B carriage by rt-PCR (Table 4).

Within-Individual Changes in Carriage Over Time

In total, 615 students participated in multiple carriage evaluation rounds: 436 participated twice, 144 participated 3 times, and 35 participated in all 4 rounds. A total of 436 (71%) were not carrying any meningococcal bacteria during any round; 89 (14%) were consistently carrying meningococcal bacteria during each round in which they participated, though not necessarily the same strain or serogroup; no single individual remained a carrier during all 4 rounds. Fifty (8%) were carrying meningococcal bacteria during 1 round but were not carrying any meningococci during a later round, indicating they lost carriage; 45 (7%) did not have carriage but then acquired carriage that was detected during a later round.

Of the 50 students who lost meningococcal carriage, 13 lost carriage after 1 MenB-FHbp dose, 32 after 2 doses, and 5 after 3 doses. Of the 45 students who acquired meningococcal carriage, 20 acquired carriage after 1 MenB-FHbp dose, 16 after 2 doses, and 9 after 3 doses. During the evaluation, 11 students lost serogroup B carriage by rt-PCR: 2 after 1 MenB-FHbp dose, 8 after 2 doses, and 1 after 3 doses. In total, 10 students acquired serogroup B carriage by rt-PCR: 3 after 1 MenB-FHbp dose, 4 after 2 doses, and 3 after 3 doses.

Outbreak Strain

Only 1 individual was found to carry the outbreak sequence type, ST-9069, during this evaluation. This student participated in only rounds 2 and 3, was carrying ST-9069 during both rounds, and had received 1 dose of MenB-FHbp by round 2 and 2 doses by round 3. Like the disease-causing strain, the carried strain was serogroup B by rt-PCR. However, the

carried strain was nongroupable by slide agglutination due to phase variation in the capsule locus.

DISCUSSION

In each carriage evaluation round, 20%–24% of participating students were carrying meningococcal bacteria, and 4% specifically carried serogroup B by rt-PCR. This overall meningococcal carriage prevalence is comparable to previously reported prevalences of up to 34% among university students in the United Kingdom [23], a country with higher meningococcal disease incidence than the United States. However, the observed carriage prevalence was higher than recent US estimates of 1%–8% among persons in nonuniversity outbreak settings [24, 25].

Despite the high carriage prevalence, most carried strains were nongroupable and therefore less likely to be invasive; no further meningococcal disease cases associated with Providence College have occurred; and only 1 carrier of the outbreak sequence type was identified. The carried strain was nongroupable by slide agglutination due to phase variation in the capsule locus. It is unclear whether the bacteria stopped expressing capsule *in vivo*, perhaps contributing to the observed prolonged carriage of this strain, or whether the bacteria changed expression during culture *in vitro*, prior to slide agglutination testing. Carried meningococcal strains may temporarily downregulate capsular expression to enhance their ability to colonize the nasopharynx and evade the human immune response; capsular expression may return to help protect the bacterium during transmission [5].

As overall meningococcal carriage and serogroup B carriage remained stable during the year following initiation of the MenB-FHbp vaccination campaign with high vaccination coverage, MenB-FHbp did not appear to impact carriage at the population level. Additionally, as students continued to carry and acquire both meningococcal and serogroup B carriage, even following completion of the full 3-dose series, MenB-FHbp also did not appear to eradicate or prevent carriage acquisition at the individual level. Therefore, we did not find evidence that MenB-FHbp provided herd protection in this outbreak setting. These results are specific to MenB-FHbp and do not predict impact of other MenB vaccines on carriage. MenB-4C reduced carriage of any meningococcal bacteria by 18% (95% CI, 3%–31%) by 3 months after completion of the 2-dose series but had no effect specifically on serogroup B carriage [23]. High coverage of MenACWY vaccination may have impacted carriage in our study, as only 5 isolates expressing serogroup A, C, W, or Y capsules were detected.

Risk factors associated with increased carriage in this evaluation were similar to those previously reported, in particular male sex [26, 27], smoking [26, 28, 29], and social mixing [30]; recent antibiotic use was associated with decreased carriage [26]. The prevalence of reported smoking was elevated, as 21%–30% of participants per round reported smoking compared to the 16.7% of adults aged 18–24 years nationally who reported smoking cigarettes in 2014 [31]. Second-hand smoke and recent upper respiratory infection symptoms did not appear to be independent risk factors for meningococcal carriage in multivariable analyses, which is in contrast to results from some previous studies [28, 32].

While these carriage evaluation methods had high specificity due to bacterial culture followed by biochemical testing and rt-PCR, they had an unknown sensitivity; a negative carriage finding may indicate either true lack of carriage or lack of detection. Lack of detection could result from imperfect assay sensitivity; a low density of *N. meningitidis* oropharyngeal colonization in a particular person; variations in oropharyngeal swabbing technique between different carriage evaluation staff; or technical difficulties with specimen collection. The inability to distinguish between lack of carriage vs detection complicates interpretation of within-individual data over time. Additionally, this evaluation spanned 2 academic school years, separated by summer vacation in which students dispersed and intense social mixing cycles were disrupted and incoming freshmen joined the student population, further complicating data interpretation and possibly explaining the lower carriage prevalence observed in round 3.

Despite high vaccination coverage, carriage prevalence on campus remained stable, suggesting MenB-FHbp does not rapidly reduce either overall or serogroup B meningococcal carriage or prevent serogroup B carriage acquisition at the individual level. Lack of impact of MenB-FHbp on carriage and therefore herd protection reinforces the need to achieve high vaccination coverage to protect vaccinated individuals as well as antimicrobial chemoprophylaxis for close contacts during outbreaks [6]. These findings can inform MenB vaccination guidelines for adolescents and young adults, particularly in outbreak settings. Additional molecular analyses are underway to further characterize the carriage isolates, compare carriage vs invasive isolates, examine within-individual changes in carriage over time, and investigate MenB vaccine antigens among the carriage isolates.

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Table 1

Meningococcal Carriage Evaluation Timing and Participant Characteristics

Carriage evaluation round	Round 1: February 2015, N (%)	Round 2: April 2015, N (%)	Round 3: September 2015, N (%)	Round 4: March 2016, N (%)
	Baseline/5–12 Days after Dose 1	Dose 2	Upperclassmen: Dose 3 Freshmen: Dose 1	One Year Post- Outbreak Freshmen: Dose 3
Participant characteristic				
Graduation year				
2019	0 (0)	0 (0)	50 (8) ^a	322 (51) ^a
2018	192 (27)	239 (27)	204 (33)	99 (16)
2017	283 (39)	250 (28)	134 (22)	97 (16)
2016	118 (16)	192 (22)	198 (32)	106 (17)
2015	121 (17)	194 (22)	27 (4) ^b	0 (0) ^b
Graduate student	3 (0.4)	3 (0.3)	9 (2)	2 (0.3)
Live on campus	655 (91)	734 (84)	452 (73)	557 (89)
Male	247 (34)	353 (40)	263 (42)	230 (37)
Recent antibiotic use ^c	106 (15)	90 (10)	59 (9)	57 (9)
Recent upper respiratory symptoms ^d	397 (55)	274 (31)	105 (17)	187 (30)
Smoker ^c	154 (21)	252 (29)	187 (30)	148 (24)
Second-hand smoke ^c	260 (36)	441 (50)	318 (51)	278 (44)
Visit bars, clubs, parties 1×/wk	532 (74)	600 (68)	417 (67)	438 (70)
Received MenACWY vaccine ^e	696 (97)	845 (96)	570 (92)	583 (93)
Received MenB-FHbp vaccine doses ^e				
0	717 (100)	11 (1)	109 (18)	37 (6)
1	0 (0)	867 (99)	12 (2)	82 (13)
2	0 (0)	0 (0)	501 (81)	338 (54)
3	0 (0)	0 (0)	0 (0)	169 (27)
Total	717	878	622	626

Abbreviations: MenACWY, quadrivalent meningococcal conjugate vaccine; MenB-FHbp, serogroup B meningococcal.

^aIncoming freshmen.

^b Graduated seniors who were invited back to campus to receive the third vaccine dose.

^c In the past 30 days.

^d In the past 2 weeks.

^e Refers to vaccine doses received 2 weeks prior to date of specimen collection.

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Table 2

Meningococcal Carriage and Serogroups

Meningococcal Carriage	Round 1: February 2015, N (%)	Round 2: April 2015, N (%)	Round 3: September 2015, N (%)	Round 4: March 2016, N (%)
Total participants	717	878	622	626
<i>Neisseria meningitidis</i> carriage	175 (24)	211 (24)	123 (20)	130 (21)
Meningococcal serogroup				
By real-time polymerase chain reaction ^a				
A	0 (0)	0 (0)	0 (0)	0 (0)
B	31 (4)	36 (4)	26 (4)	22 (4)
C	8 (1)	3 (0.3)	0 (0)	0 (0)
W	0 (0)	0 (0)	1 (0.2)	1 (0.2)
X	1 (0.1)	2 (0.2)	0 (0)	5 (1)
Y	3 (0.4)	4 (0.5)	1 (0.2)	2 (0.3)
Nongroupable	132 (18)	166 (19)	95 (15)	100 (16)
By slide agglutination ^b				
A	0 (0)	0 (0)	0 (0)	0 (0)
B	9 (1)	12 (1)	7 (1)	6 (1)
C	1 (0.1)	0 (0)	0 (0)	0 (0)
E ^c	4 (1)	4 (0.5)	6 (1)	8 (1)
W	0 (0)	0 (0)	0 (0)	0 (0)
X	3 (0.4)	2 (0.2)	0 (0)	0 (0)
Y	2 (0.3)	2 (0.2)	0 (0)	0 (0)
Z ^c	0 (0)	0 (0)	1 (0.2)	0 (0)
Nongroupable	156 (22)	191 (22)	109 (18)	116 (19)

^aIn round 1, 18% of 175 isolates were serogroup B, 5% were serogroup C, 1% were serogroup X, 2% were serogroup Y, and 75% were nongroupable by real-time polymerase chain reaction. Similarly, round 2 isolates were 17% B, 1% C, 1% X, 2% Y, and 79% nongroupable; round 3 isolates were 21% B, 1% W, 1% Y, and 77% nongroupable; and round 4 isolates were 17% B, 1% W, 4% X, 2% Y, and 77% nongroupable.

^bIn round 1, 5% of 175 isolates were serogroup B, 1% were serogroup C, 2% were serogroup E, 2% were serogroup X, 1% were serogroup Y, and 89% were nongroupable by slide agglutination. Similarly, round 2 isolates were 6% B, 2% E, 1% X, 1% Y, and 91% nongroupable; round 3 isolates were 6% B, 5% E, 1% Z, and 89% nongroupable; and round 4 isolates were 5% B, 6% E, and 89% nongroupable.

^cSerogroups E and Z were only assessed via slide agglutination, not by real-time polymerase chain reaction.

Table 3

Associations With Any Meningococcal Carriage

Characteristic	Bivariate Prevalence Ratio ^a	P Value	Multivariable Prevalence Ratio ^{a,b}	P Value
Round				
1	1.0		1.0	
2	1.1 (0.9, 1.2)	.351	0.7 (0.4, 1.1)	.111
3	0.8 (0.7, 1.0)	.033	0.6 (0.4, 0.9)	.013
4	0.9 (0.8, 1.1)	.261	0.6 (0.4, 1.0)	.062
Graduation year				
2019	1.0 (0.7, 1.4)	.985	1.1 (0.8, 1.7)	.503
2018	1.0		1.0	
2017	1.6 (1.3, 1.9)	<.001	1.5 (1.2, 1.9)	<.001
2016	1.3 (1.0, 1.6)	.067	1.2 (1.0, 1.5)	.107
2015	0.9 (0.7, 1.2)	.515	0.9 (0.7, 1.2)	.608
Graduate student	0.7 (0.1, 4.2)	.670	0.8 (0.2, 4.1)	.837
Live on campus	0.9 (0.8, 1.1)	.544	—	—
Male	1.5 (1.3, 1.8)	<.001	1.3 (1.1, 1.5)	<.001
Recent antibiotic use ^c	0.4 (0.3, 0.6)	<.001	0.4 (0.3, 0.6)	<.001
Recent upper respiratory symptoms ^d	1.1 (1.0, 1.2)	.064	—	—
Smoker ^c	1.5 (1.3, 1.7)	<.001	1.3 (1.1, 1.5)	.003
Second-hand smoke ^c	1.2 (1.1, 1.4)	.006	1.0 (0.8, 1.1)	.610
Visit bars, clubs, parties 1×/wk	1.9 (1.6, 2.2)	<.001	1.8 (1.5, 2.1)	<.001
Received MenACWY vaccine ^e	1.1 (0.8, 1.6)	.633	—	—
Received MenB-FHbp vaccine doses ^e				
0	1.0		1.0	
1	1.8 (1.1, 2.8)	.014	1.5 (1.0, 2.4)	.074
2	1.5 (1.0, 2.1)	.037	1.4 (1.0, 2.1)	.082
3	1.8 (1.1, 2.9)	.015	1.6 (0.9, 2.7)	.124

A total of 2843 observations from 2014 unique individuals were included in these models.

Abbreviations: MenACWY, quadrivalent meningococcal conjugate vaccine; MenB-FHbp, serogroup B meningococcal factor H binding protein.

^aPrevalence ratios account for repeat participants using generalized estimating equation methods.

^bVariables with significance >0.05 in bivariate models were not included in the multivariable model.

^cIn the past 30 days.

^dIn the past 2 weeks.

^eRefers to vaccine doses received 2 weeks prior to date of specimen collection.

Table 4

Associations With Serogroup B Carriage by Real-Time Polymerase Chain Reaction

Characteristic	Bivariate Prevalence Ratio ^a	P Value	Multivariable Prevalence Ratio ^{a,b}	P Value
Round				
1	1.0		1.0	
2	1.0 (0.7, 1.4)	.932	0.5 (0.2, 1.8)	.327
3	0.9 (0.6, 1.4)	.712	0.7 (0.3, 1.5)	.352
4	0.8 (0.5, 1.3)	.304	0.4 (0.1, 1.7)	.200
Graduation year				
2019	3.0 (1.2, 7.3)	.015	3.6 (1.1, 11.6)	.029
2018	1.0		1.0	
2017	2.5 (1.3, 4.8)	.008	2.5 (1.3, 4.8)	.009
2016	2.9 (1.5, 5.8)	.002	2.8 (1.4, 5.6)	.003
2015	1.7 (0.8, 3.9)	.184	1.8 (0.8, 4.0)	.169
Graduate student	6.1 (0.9, 41.4)	.066	7.6 (1.5, 39.9)	.016
Live on campus	0.7 (0.5, 1.2)	.231	—	—
Male	1.9 (1.3, 2.7)	.002	1.6 (1.0, 2.4)	.037
Recent antibiotic use ^c	0.4 (0.2, 0.8)	.015	0.4 (0.2, 0.9)	.032
Recent upper respiratory symptoms ^d	1.1 (0.9, 1.3)	.368	—	—
Smoker ^c	1.8 (1.3, 2.6)	.001	1.5 (1.0, 2.2)	.047
Second-hand smoke ^c	1.5 (1.1, 2.1)	.007	—	—
Visit bars, clubs, parties 1x/wk	1.6 (1.1, 2.3)	.016	1.5 (1.0, 2.3)	.043
Received MenACWY vaccine ^e	0.6 (0.3, 1.3)	.182	—	—
Received MenB-FHbp vaccine doses ^e				
0	1.0		1.0	
1	1.4 (0.4, 4.6)	.599	1.8 (0.6, 5.8)	.329
2	0.9 (0.5, 1.8)	.829	1.3 (0.6, 2.8)	.567
3	0.9 (0.3, 2.7)	.887	1.8 (0.4, 8.7)	.489

A total of 2843 observations from 2014 unique individuals were included in these models.

Abbreviations: MenACWY, quadrivalent meningococcal conjugate vaccine; MenB-FHbp, serogroup B meningococcal factor H binding protein.

^aPrevalence ratios account for repeat participants using generalized estimating equation methods.

^bVariables with significance >0.05 in bivariate models were not included in the multivariable model. Round and received MenB-FHbp doses were retained, as these were primary variables of interest.

^cIn the past 30 days.

^dIn the past 2 weeks.

^eRefers to vaccine doses received 2 weeks prior to date of specimen collection.