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Meningococcal Carriage Following a University Serogroup B Meningococcal Disease Outbreak and Vaccination Campaign with MenB-4C and MenB-FHbp — Oregon, 2015–2016

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Abstract

Background—Limited data exist on the impact of the serogroup B meningococcal (MenB) vaccines MenB-FHbp and MenB-4C on meningococcal carriage and herd protection. We therefore assessed meningococcal carriage following a MenB vaccination campaign in response to a university serogroup B meningococcal disease outbreak in 2015.

Methods—A convenience sample of students recommended for vaccination provided oropharyngeal swabs and completed questionnaires during four carriage surveys over 11 months. Isolates were tested by real-time PCR, slide agglutination, and whole genome sequencing. Vaccination history was verified via university records and the state immunization registry.

Results—A total of 4,225 oropharyngeal swabs were analyzed from 3,802 unique participants. Total meningococcal and genotypically serogroup B carriage prevalence among sampled students were stable at 11–17% and 1.2%–2.4% during each round, respectively; no participants carried the outbreak strain. Neither 1–3 doses of MenB-FHbp nor 1–2 doses of MenB-4C was associated with decreased total or serogroup B carriage prevalence.

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Conclusions—While few participants completed the full MenB vaccination series, limiting analytic power, these data suggest that MenB-FHbp and MenB-4C do not have a large, rapid impact on meningococcal carriage and are unlikely to provide herd protection in the context of an outbreak response.

Keywords

Meningococcal disease; *Neisseria meningitidis*; carriage; vaccination; MenB-4C; MenB-FHbp; outbreak response

Introduction

In January–May, 2015, six cases of serogroup B meningococcal disease, including one death, occurred among undergraduate students at a large Oregon university (~20,000 undergraduates). One additional, non-fatal case occurred in a close contact of a student. All cases were caused by the same strain of *Neisseria meningitidis* serogroup B: clonal complex 32, sequence type (ST) 32. In response to the outbreak, local public health officials provided the serogroup B meningococcal (MenB) vaccine MenB-4C (Bexsero®, GlaxoSmithKline, two-dose series) to a small number of interested students beginning in February 2015. Subsequently, mass vaccination campaigns with MenB-FHbp (Trumenba®, Pfizer, three-dose series recommended for outbreak response) were held in March, May, and October 2015 and February 2016. MenB-FHbp was also available at local pharmacies throughout this time period and during freshmen orientation (June–August 2015). At least 25% of undergraduate students received at least one dose of MenB-FHbp or MenB-4C at the mass vaccination clinics (Fisher et al., manuscript in preparation); however, due to the many additional opportunities for students to receive vaccine, overall vaccination coverage at the university was likely substantially higher.

Meningococcal disease is a serious illness with a 10–20% case-fatality ratio; however, only 433 cases were reported in the United States in 2014 (incidence: 0.18 per 100,000 population) [1]. In addition to causing disease, meningococci are frequently carried asymptomatically in the nasopharynx. Asymptomatic meningococcal carriage is not a risk factor for meningococcal disease; rather, carriage and disease are distinct outcomes of meningococcal acquisition [2]. However, because carriers are an important source of transmission, population meningococcal carriage must be reduced to provide herd protection against meningococcal disease. Serogroup C and A conjugate meningococcal vaccines have been shown to provide herd protection against the specific serogroups targeted by the vaccines [3,4].

In the United States, conjugate meningococcal vaccines that protect against serogroups A, C, W, and Y (MenACWY) were approved in 2005 and are routinely administered to adolescents [5]. The MenB vaccines MenB-FHbp and MenB-4C were licensed in the US in 2014–2015 as a 2 (MenB-4C) or 2–3 (MenB-FHbp) dose series for persons aged 10–25 [6]. Because these vaccines contain meningococcal outer membrane proteins present in both serogroup B and non-serogroup B meningococci, they could potentially impact carriage of all meningococci, not just serogroup B. However, only two studies of MenB vaccine impact

on meningococcal carriage have been published. One study found an 18% reduction in overall meningococcal carriage (95% confidence interval 3–31%) among university students vaccinated with MenB-4C; however, no impact on serogroup B carriage was observed [7]. The other study assessed carriage following mass vaccination with MenB-FHbp at a university; no reduction in overall or serogroup B carriage in the population was observed [8].

During the Oregon university outbreak, it was believed that both MenB-FHbp and MenB-4C would help protect individual students from developing disease due to the outbreak strain. However, it was not known whether MenB vaccination would impact meningococcal carriage and transmission to provide herd protection in this population. We implemented a meningococcal carriage evaluation in conjunction with the vaccination clinics to assess the prevalence of meningococcal carriage in this population and evaluate the impact of the vaccination campaign on carriage of (1) any meningococci, (2) serogroup B *N. meningitidis*, and (3) the strain associated with the outbreak.

Methods

This evaluation was considered non-research, public health evaluation by CDC and Oregon Health Authority and did not require institutional review for human subjects' protection. Four carriage evaluation rounds were conducted in conjunction with the mass vaccination clinics held in March, May, and October 2015 and February 2016. All students at the affected university who were recommended to receive MenB vaccine were eligible to participate in the carriage evaluation; this included all undergraduate students as well as graduate students living in undergraduate dormitories or with medical conditions that increase the risk for meningococcal disease (persistent complement component deficiency or functional or anatomic asplenia) [6]. Students were eligible to participate in the carriage evaluation regardless of whether they had received MenB vaccine and could participate in multiple evaluation rounds, but only once per round.

A convenience sample of students was recruited at mass vaccination clinics during a 15-minute post-vaccination waiting period and at high-traffic sites on the university campus. Participants provided informed consent and completed a short questionnaire assessing demographics, vaccination status, and risk factors for meningococcal disease. Trained staff swabbed each participant's tonsils and posterior oropharynx using a polyester double swab (BD BBL; Franklin Lakes, NJ, US). Swabs were immediately plated on Modified Thayer-Martin (MTM) agar (BD BBL; Franklin Lakes, NJ, US) and stored at room temperature in Mitsubishi boxes in CO_2 atmosphere for a maximum of 4 hours before transport to the laboratory, where they were incubated at 37°C with 5% CO_2.

The plates were examined for growth at 24, 48, and 72 hours. Colonies with typical *Neisseria* morphology were subcultured onto blood agar (BD BBL; Franklin Lakes, NJ, US) and tested by Gram Stain (BD BBL; Franklin Lakes, NJ, US); oxidase test (Hardy Diagnostics; Santa Maria, CA, US) was performed on subcultured colonies of all Gram-negative diplococci from the blood agar plate. When oxidase-positive, Gram-negative diplococci were found, API NH strip (bioMerieux; Durham, NC, US) and real-time

polymerase chain reaction (rt-PCR) for *sodC* were used to confirm species [9]; discrepancies between tests were resolved through whole genome sequencing (WGS). Remaining colonies were subcultured and further characterized by slide agglutination (SASG) using commercially available antisera (DIFCO, BD BBL; Franklin Lakes, NJ, US) for expression of the serogroup A, B, C, W, X, and Y capsule antigens [10]; and singleplex rt-PCR for serogroup A, B, C, W, X, and Y capsule biosynthesis genes [10,11]. Isolates were classified as nongroupable by rt-PCR if the capsule biosynthesis genes for these six serogroups were not detected. Isolates negative for serogroup A, B, C, W, X, and Y capsule antigen expression by SASG were classified as "other" as these isolates could either be phenotypically nongroupable or could express the non-disease associated serogroup E or Z capsule antigens.

WGS was performed on serogroup B isolates identified using SASG or rt-PCR to determine similarity to the university outbreak strain. Genomic DNA was extracted using the ArchivePure™ DNA purification kit (5 Prime, Gaithersburg, MD, US) to create libraries for sequencing using the NEBNext Ultra DNA library preparation kit (New England Biolabs Inc., Ipswich, MA, US). Sequencing was performed using an Illumina MiSeq with MiSeq 250-bp paired-end kits (Illumina, San Diego, CA, US). Raw sequence reads with high quality were trimmed and assembled using CLC Bio Genomics Workbench (v8.5.1, Qiagen, Waltham, MA, US) as previously described [12]. A BLAST search was used on the assembled genomes and compared with PubMLST to identify multilocus sequence typing (MLST) alleles [13,14]. For serogroup B isolates, *porA* and *porB* antigenic sequences were also assessed to characterize similarity to the outbreak strain.

Student meningococcal vaccination history was verified using university student health medical records, vaccination clinic attendance registers, and the Oregon state immunization registry, ALERT IIS.

Statistical analysis was conducted using SAS 9.3 (Cary, NC). We performed descriptive statistics of patient characteristics and calculated prevalence ratios (PRs) for associations between participant characteristics and overall or serogroup B meningococcal carriage. Bivariate and multivariable analysis was conducted using Poisson regression with generalized estimating equations (GEE) to account for individuals participating in multiple rounds. Where possible, we used an unstructured correlation matrix; for models that did not converge we instead used an autoregressive correlation matrix. Multivariable models included all variables that were significant ($p<0.05$) in bivariate analysis as well as MenB vaccination status. A descriptive analysis of within-individual changes in carriage was performed for individuals who participated in multiple carriage evaluation rounds. We included only MenB vaccine doses received ≥14 days prior to carriage evaluation participation to ensure that we did not include doses that had been received too recently to have stimulated an immune response.

Results

A total of 4,526 participants were enrolled over four carriage evaluation rounds. Of these, 301 were excluded: 14 due to ineligibility; 284 because their swab could not be tested due to

laboratory equipment failure (n=265), plating error, contamination, or missing sample; and 3 because consent forms or questionnaires were missing. This resulted in a total of 4,225 oropharyngeal swabs analyzed from 3,802 unique participants. A total of 328 students participated in more than one evaluation round: 247 participated in two rounds, 77 in three rounds, and four participated in four rounds. Table 1 summarizes participant characteristics (participants missing information for each characteristic are not shown).

No individual source of meningococcal vaccination history was complete; however, based on student self-report and vaccine history abstraction, MenACWY vaccination status could be assigned for 3431/4225 (81%) participants and MenB vaccination status for 3732/4225 (88%) (Table 1). MenACWY vaccination status was validated from written records for 2854/4225 participants (68%) and MenB vaccination status was validated for 3063/4225 (72%); remaining participants had vaccination status assigned based on self-report alone. Of participants with assigned MenACWY vaccination status, 82% had received MenACWY vaccine; of participants with assigned MenB vaccination status, 57% had received one or more doses of a MenB vaccine ≥14 days prior to carriage evaluation participation (Table 1). Including both documented and self-reported vaccination status, 64 participants (1.7%; all unique participants) received a complete three-dose series of MenB-FHbp and 135 (3.6%; 133 unique participants) received a complete two-dose series of MenB-4C (Table 1).

Meningococcal carriage was found in 11%–17% of participants in each round, with highest carriage in rounds 2 and 4 (Table 2). Most carried meningococci did not express serogroup A, B, C, W, X, or Y capsule antigens (per SASG) and were genotypically (by rt-PCR) nongroupable (Table 2). In each round, approximately 1%–2% of students carried genotypically serogroup B *N. meningitidis* and bacteria expressing the serogroup B capsule were carried by <1% of participants (Table 2). Carriage of serogroups C, W, X, and Y was <1% by rt-PCR and <0.5% by SASG (Table 2).

MLST sequence type could be assessed through WGS for 78/79 serogroup B isolates. Two ST-32 serogroup B isolates were identified (Table 3); however, comparison of *porA* and *porB* antigenic sequences demonstrated that the carried isolates did not match the outbreak strain. The remaining 76 serogroup B isolates represented a wide variety of STs. ST-136 was the most frequently detected (n=27) (Table 3).

In bivariate analyses, increased carriage of any *N. meningitidis* was associated with participation during rounds 2 or 4; male gender; sophomore or junior year; age 19–22 years; living off-campus; living in an apartment, house, sorority, or fraternity; having ≥3 roommates; upper respiratory tract infection symptoms in the past 30 days; recent smoking or second-hand smoke exposure; and attending parties, bars, clubs, or other social mixing events ≥ once per week (Table 4). Living with family and recent antibiotic use were associated with lower carriage (Table 4). In multivariable analysis, male sex, being 20 years of age, smoking, and attending social mixing events ≥ once per week remained associated with increased carriage and recent antibiotic use with decreased carriage (Table 4).

Receipt of two MenB-4C doses was associated with increased carriage in bivariate analysis; however, no association between meningococcal carriage and MenB-FHbp or MenB-4C was

observed in multivariable analysis (Table 4). Further analysis showed that MenB-4C receipt was associated with increased frequency of social mixing and having ≥3 roommates (data not shown). Similar results were obtained when the analysis was restricted to participants for whom MenB vaccinations could be verified through university records or the state immunization registry (data not shown).

Associations between participant characteristics and carriage of genotypically serogroup B meningococci were also assessed. Round 2; age 19, 20, or 22 years; having ≥3 roommates; smoking; and attending social mixing events 2–3 times per week were associated with increased serogroup B carriage in bivariate analysis (Table 5). Smoking and social mixing remained associated with increased serogroup B carriage in the multivariable analysis (Table 5). Receipt of MenB-FHbp or MenB-4C was not associated with serogroup B carriage in either bivariate or multivariable analysis (Table 5). Similar results were again obtained when the analysis was restricted to participants for whom MenB vaccinations could be verified through university records or the state immunization registry (data not shown).

We also evaluated changes in carriage between rounds for individuals who participated in multiple rounds. After classifying participants by the type and number of MenB vaccine doses received prior to their second participation time point, only 18 individuals in the longitudinal analysis had not received any MenB vaccine doses by their second round of participation (Table 6). None of these 18 individuals carried *N. meningitidis* during either their first or their second round of participation (Table 6), meaning that carriage loss among vaccinated and unvaccinated individuals could not be compared. Meningococcal carriage acquisition was observed in 5–11% of individuals who had received 1–3 doses of MenB-FHbp or 1–2 doses of MenB-4C (Table 6); however, carriage acquisition among vaccinated and unvaccinated groups also could not be compared due to small numbers. Three individuals acquired genotypically serogroup B (phenotypically nongroupable) meningococci; all other individuals with new carriage acquired genotypically nongroupable meningococci.

Discussion

The four meningococcal carriage evaluation rounds spanned 11 months, beginning in the middle of the outbreak and ending nine months after the last outbreak case occurred. During this period, no decrease in overall or serogroup B meningococcal carriage was observed among sampled students, suggesting that the mass vaccination campaign at the university did not substantively reduce meningococcal transmission within the population. Overall meningococcal carriage was lower during the third evaluation round; however, this round occurred shortly after students returned from summer break, a period during which more limited opportunities for student interaction may have resulted in reduced meningococcal transmission within the population. By round 4 carriage had increased above baseline carriage in round 1. In the multivariable analysis, differences in carriage by round were not statistically significant.

Our analysis also did not reveal any association between vaccination and overall or serogroup B meningococcal carriage at the individual level, although the low carriage

prevalence of serogroup B meant that power to detect associations with serogroup B carriage was limited. Overall, these findings suggest that neither MenB-4C nor MenB-FHbp had a large, rapid impact on meningococcal carriage that could provide herd protection in the context of a meningococcal disease outbreak. However, as relatively few participants had received MenB-4C or completed a full MenB vaccination series with either vaccine, power to detect moderate changes in carriage following receipt of the full vaccination series was also limited. It remains possible that the MenB vaccines could have a longer-term impact on carriage following administration of the complete vaccination series. Furthermore, MenB vaccination is still the best way to provide individual protection for the duration of the outbreak to people in the affected population.

Carriage of the outbreak strain was not detected during any round of the carriage evaluation. However, as three outbreak cases occurred after the first carriage evaluation round occurred, it is clear that the outbreak strain was still circulating within the university population, but with a low enough prevalence that it was not observed in the sampled population. Low outbreak strain carriage has been found in other meningococcal disease outbreaks [8,15], and suggests that acquisition of pathogenic strains associated with outbreaks is more likely to lead to disease and less likely to lead to carriage; or if carriage is established, the duration of carriage may be relatively short [16].

The meningococcal carriage prevalence of 11–17% observed here is similar to that found in another recent university carriage evaluation in the United States [8]; however, both studies showed higher carriage prevalence than that observed in other recent US carriage evaluations [15,17,18]. These other evaluations recruited participants from high schools [17] or the general population [15,18] rather than restricting participation to university students. Meningococcal carriage has previously been associated with social mixing [19] and age [20,21], so it is not surprising that relatively high carriage was detected among university undergraduates. As very little carriage of serogroup B ST-32 was detected, it is also unlikely that the relatively high carriage prevalence is related to the historically higher rates of meningococcal disease due to serogroup B ST-32 in Oregon [22]. Substantially higher carriage prevalence of ≥30%, including up to 18% carriage prevalence of disease-associated serogroups, has been detected among university students in the United Kingdom [7,23].

Interestingly, both our evaluation and the recent evaluation by Soeters et al. [8] detected carriage prevalence of *N. meningitidis* expressing the B, C, or Y capsular polysaccharide that was similar to or lower than that observed previously in the United States [15,17]. The higher total meningococcal carriage prevalence in our sample was instead due to high carriage of phenotypically and genotypically nongroupable meningococci, which were detected in 10–17% of participants in each round. The low carriage of encapsulated serogroup C, W, and Y meningococci (0–0.4% of participants per round) in a setting of high overall meningococcal carriage could be related to routine use of MenACWY vaccines in US adolescents. However, due to the extremely low carriage of these serogroups among our participants, we could not assess the potential relationship between MenACWY vaccination and carriage.

Vaccinated and unvaccinated students included in this observational evaluation may be substantially different in characteristics that may affect risk of carriage. Indeed, students who received MenB-4C reported a significantly higher frequency of social mixing than students who did not receive a MenB vaccine. While we controlled for confounding by assessing meningococcal carriage risk factors through our questionnaire and including these factors in the multivariable analysis, unidentified confounding could obscure an association between MenB vaccination and meningococcal carriage. We also had limited longitudinal data to assess meningococcal carriage acquisition and loss in our participants, so we could not assess whether the MenB vaccines impact meningococcal carriage loss or acquisition more than overall carriage.

Although analytical power was limited by the relatively few participants who completed a MenB vaccination series, our findings suggest that neither MenB-FHbp nor MenB-4C vaccination has a large, rapid effect on meningococcal carriage. This suggests that using these vaccines during a meningococcal disease outbreak is unlikely to rapidly provide herd protection in the target population. Without herd protection, high vaccination coverage in the population at risk is essential to help protect each individual at increased risk; meanwhile, chemoprophylaxis of close contacts of meningococcal disease cases remains critical to reduce transmission and prevent secondary cases [5]. This evaluation will inform MenB vaccination guidelines; however, additional information on the effectiveness, coverage, and duration of protection afforded by both MenB vaccines is needed to develop the best guidelines for their use.

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Summary

Following a serogroup B meningococcal disease outbreak at an Oregon university, a meningococcal carriage evaluation was conducted in conjunction with a MenB-FHbp and MenB-4C vaccination campaign. Neither vaccine was associated with reduced meningococcal carriage among participants.

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Table 1

Characteristics of carriage evaluation participants at an Oregon university, March 2015–February 2016

Characteristic[1]	Round 1: March 2015, N (%)	Round 2: May 2015, N (%)	Round 3: October 2015, N (%)	Round 4: February 2016, N (%)	TotalN (%)
Total participants	**1173**	**1069**	**1045**	**938**	**4225**
Gender (n=4131)					
Male	503 (44)	426 (41)	404 (39)	358 (39)	**1691 (41)**
Year in school (n=4163)					
Freshman	281 (25)	295 (28)	420 (41)	409 (44)	**1406 (34)**
Sophomore	271 (24)	246 (23)	206 (20)	142 (15)	**865 (21)**
Junior	283 (25)	252 (24)	181 (17)	147 (16)	**863 (21)**
Senior	303 (27)	263 (25)	212 (20)	184 (20)	**962 (23)**
Graduate student	3 (0.3)	8 (0.8)	16 (1.6)	40 (4.3)	**67 (1.6)**
Age (n=4194)					
18	146 (13)	103 (9.7)	374 (36)	240 (26)	**863 (21)**
19	275 (24)	292 (28)	210 (20)	250 (27)	**1027 (43)**
20	256 (22)	221 (21)	160 (15)	122 (13)	**759 (18)**
21	222 (19)	192 (18)	145 (14)	124 (13)	**683 (16)**
22	135 (12)	149 (14)	61 (5.8)	74 (8.0)	**419 (10)**
23–29	104 (9.0)	95 (9.0)	77 (7.4)	102 (11)	**378 (9.0)**
30+	19 (1.6)	10 (0.9)	17 (1.6)	19 (2.0)	**65 (1.5)**
Live on vs. off-campus (n=3961)					
On-campus	273 (27)	326 (31)	427 (42)	411 (46)	**1437 (34)**
Type of residence (n=3809)					
Residence hall	279 (31)	312 (30)	410 (42)	397 (45)	**1398 (37)**
Apartment/house	590 (65)	662 (64)	561 (57)	454 (52)	**2267 (60)**
Sorority/fraternity	43 (4.7)	58 (5.6)	17 (1.7)	26 (3.0)	**144 (3.8)**
Roommates (n=3765)					
0	89 (10)	126 (12)	75 (7.6)	68 (7.9)	**358 (9.5)**
1	346 (39)	407 (40)	515 (52)	477 (56)	**1745 (46)**

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Characteristic[1]	Round 1: March 2015, N (%)	Round 2: May 2015, N (%)	Round 3: October 2015, N (%)	Round 4: February 2016, N (%)	TotalN (%)
2	134 (15)	136 (13)	123 (12)	93 (11)	**486 (13)**
3+	266 (30)	309 (30)	221 (22)	177 (21)	**973 (26)**
Live with family	57 (6.4)	49 (4.8)	56 (5.7)	41 (4.8)	**203 (5.4)**
Recent upper respiratory symptoms[2] (n=4166)					
Yes	527 (46)	324 (31)	348 (34)	361 (39)	**1560 (37)**
Smoking[3] (n=4142)					
Yes	396 (35)	326 (31)	339 (33)	305 (33)	**1366 (33)**
Second-hand smoke[3] (n=4163)					
Never	531 (46)	470 (45)	472 (46)	456 (49)	**1929 (46)**
Some days	564 (49)	541 (52)	513 (50)	451 (49)	**2069 (50)**
Every day	66 (5.7)	34 (3.3)	46 (4.5)	19 (2.1)	**165 (4.0)**
Recent antibiotic use[3] (n=4104)					
Yes	134 (12)	74 (7.1)	91 (8.9)	84 (9.2)	**383 (9.2)**
Attend bars, clubs, parties (n=4177)					
<1/week or never	574 (49)	548 (52)	610 (59)	536 (58)	**2268 (54)**
1/week	315 (27)	292 (28)	276 (27)	235 (26)	**1118 (27)**
2–3/week	242 (21)	193 (18)	130 (13)	137 (15)	**702 (17)**
≥4/week	34 (2.9)	23 (2.2)	19 (1.8)	13 (1.4)	**89 (2.1)**
Received MenACWY vaccine (n=3431)					
Yes	809 (83)	736 (84)	683 (81)	592 (80)	**2820 (82)**
Received MenB vaccine doses[4] (n=3732)					
0	1006 (100)	40 (4.6)	349 (35)	223 (26)	**1618 (43)**
1 dose MenB-FHbp	1 (0.1)	756 (87)	277 (28)	221 (26)	**1255 (34)**
2 doses MenB-FHbp	2 (0.2)	10 (1.2)	291 (29)	296 (35)	**599 (16)**
3 doses MenB-FHbp	0 (0)	0 (0)	11 (1.1)	53 (6.2)	**64 (1.7)**
1 dose MenB-4C	2 (0.2)	17 (2.0)	21 (2.1)	21 (2.5)	**61 (1.6)**
2 doses MenB-4C	0 (0)	49 (5.6)	43 (4.3)	43 (5.0)	**135 (3.6)**

[1] Participants with missing data not shown. Total N included for each characteristic shown in parentheses next to the characteristic label.

[2] In the past 30 days

[3] In the past 2 weeks

[4] Includes only vaccine doses received ≥2 weeks before specimen collection

Table 2

Overall and serogroup-specific meningococcal carriage among carriage evaluation participants at an Oregon university, March 2015–February 2016

	Round 1: March 2015, N (%)	Round 2: May 2015, N (%)	Round 3: October 2015, N (%)	Round 4: February 2016, N (%)	TotalN (%)
N. meningitidis carriage	167 (14)	183 (17)	110 (11)	163 (17)	**622 (15)**
Serogroup					
Genotypic (rt-PCR)[1]					
B	14 (1.2)	23 (2.3)	20 (1.9)	22 (2.4)	**78 (1.8)**
C	3 (0.26)	1 (0.09)	3 (0.29)	1 (0.11)	**8 (0.19)**
W	2 (0.17)	0 (0)	0 (0)	1 (0.11)	**3 (0.07)**
X	1 (0.09)	1 (0.09)	0 (0)	0 (0)	**2 (0.05)**
Y	3 (0.26)	2 (0.19)	3 (0.29)	5 (0.53)	**13 (0.31)**
Nongroupable	144 (12)	156 (15)	84 (8.0)	134 (14)	**510 (12)**
Phenotypic (SASG)[1]					
B	3 (0.26)	5 (0.47)	3 (0.29)	5 (0.53)	**16 (0.38)**
W	1 (0.09)	0 (0)	0 (0)	1 (0.11)	**2 (0.05)**
X	0 (0)	1 (0.09)	0 (0)	0 (0)	**3 (0.07)**
Y	1 (0.09)	0 (0)	0 (0)	3 (0.32)	**5 (0.12)**
Other	162 (14)	177 (17)	107 (10)	154 (16)	**577 (14)**
Total participants	**1173**	**1069**	**1045**	**938**	**4225**

[1]Real time PCR (rt-PCR) and slide agglutination (SASG) both tested for serogroups A, B, C, W, X, and Y. For SASG, isolates were classified as “Other” if serogroup A, B, C, W, X, and Y capsule antigens were not detected; this classification includes phenotypically nongroupable bacteria as well as serogroups E and Z, which are rarely associated with disease. For rt-PCR, isolates were classified as nongroupable if serogroup A, B, C, W, X, and Y biosynthesis genes were not detected.

Table 3

Genotypic and phenotypic serogroup determination, clonal complex, and sequence type of carried *N. meningitidis* identified as serogroup B by real time PCR (rt-PCR) (N=78[1]) isolated from carriage evaluation participants at an Oregon university, March 2015–February 2016

N	Genotypic serogroup (rt-PCR)	Phenotypic serogroup (SASG)	Clonal complex	ST
1	B	NG	CC1117	11855
1	B	NG	CC1157	1157
2	B	B	CC162	162
1	B	NG	CC162	2153
1	B	B	CC174	1466
2	B	B	CC213	213
5	B	NG	CC213	213
1	B	B	CC213	3496
1	B	NG	CC213	11852
1	B	NG	CC269	3091
1	B	B	CC32/ET-5	322
1	B	NG	CC32/ET-5	322
1	B	B	CC32/ET-5	8758
2	B	NG	CC32/ET-5[2]	11395
3	B	NG	CC35	35
2	B	NG	CC35	11392
5	B	NG	CC41/44/Lineage 3	44
5	B	B	CC41/44/Lineage 3	136
22	B	NG	CC41/44/Lineage 3	136
6	B	NG	CC41/44/Lineage 3	409
1	B	NG	CC41/44/Lineage 3	1097
1	B	B	CC41/44/Lineage 3	1489
1	B	NG	CC41/44/Lineage 3	5881
1	B	NG	CC461	1946
1	B	NG	CC461	11861
2	B	NG	CC4821	11858
1	B	NG	CC53	53
2	B	NG	CC865	865
1	B	NG	unassigned	8537
1	B	B	unassigned	9069
1	B	NG	unassigned	11294
1	B	B	unassigned	11860

[1] One isolate (genotypically serogroup B, phenotypically NG) excluded as clonal complex and ST could not be determined

[2] Carried ST-32 isolates were not closely related to isolates from outbreak cases based on comparison of PorA and PorB antigenic sequences

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Table 4

Bivariate and multivariable associations with carriage of any *N. meningitidis* among carriage evaluation participants at an Oregon university, March 2015–February 2016

		Bivariate analysis[1]		Multivariable analysis (N=2723)	
	N	**Prevalence Ratio (95% CI)[2]**	**p-value**	**Prevalence Ratio (95% CI)[2]**	**p-value**
Round	4225				
1			Ref		
2		**1.2 (1.1–1.5)**	**0.01**	1.0 (0.7–1.5)	0.9
3		0.8 (0.7–1.0)	0.08	0.8 (0.6–1.1)	0.1
4		**1.2 (1.0–1.5)**	**0.02**	1.2 (0.8–1.7)	0.3
Gender	4131				
Female			Ref		
Male		**1.5 (1.3–1.7)**	**<0.0001**	**1.2 (1.0–1.5)**	**0.03**
Year in school	4163				
Freshman			Ref		
Sophomore		**1.4 (1.2–1.7)**	**0.0008**	0.8 (0.6–1.1)	0.2
Junior		**1.3 (1.0–1.5)**	**0.03**	0.7 (0.5–1.1)	0.2
Senior		1.2 (0.9–1.4)	0.2	0.8 (0.5–1.4)	0.5
Age	4194				
18			Ref		
19		**1.5 (1.2–1.9)**	**0.0004**	1.2 (0.9–1.6)	0.3
20		**1.8 (1.4–2.2)**	**<0.0001**	**1.6 (1.1–2.3)**	**0.02**
21		**1.4 (1.1–1.8)**	**0.006**	1.1 (0.7–1.8)	0.7
22		**1.4 (1.0–1.8)**	**0.04**	0.8 (0.5–1.5)	0.6
23–29		0.8 (0.5–1.1)	0.2	0.8 (0.4–1.5)	0.5
30+		0.8 (0.3–1.9)	0.6	1.8 (0.7–5.2)	0.4
Live on- vs. off-campus	3961				
On-campus			Ref		
Off-campus		**1.2 (1.1–1.5)**	**0.0008**	1.3 (0.7–2.2)	0.4

		Bivariate analysis[1]		Multivariable analysis (N=2723)	
	N	Prevalence Ratio (95% CI)[2]	p-value	Prevalence Ratio (95% CI)[2]	p-value
Type of residence	3809				
Residence hall			Ref		
Apartment/house		**1.2 (1.0–1.4)**	**0.02**	0.9 (0.5–1.8)	0.8
Sorority/fraternity		**2.5 (1.9–3.3)**	**<0.0001**	1.3 (0.7–2.4)	0.4
Roommates	3765				
0			Ref		
1		1.0 (0.7–1.3)	0.8	1.0 (0.7–1.4)	1.0
2		1.3 (0.9–1.7)	0.2	1.0 (0.7–1.5)	1.0
3+		**1.5 (1.1–2.0)**	**0.003**	1.2 (0.8–1.7)	0.3
Live with family		**0.4 (0.2–0.7)**	**0.0005**	0.6 (0.3–1.4)	0.2
Recent upper respiratory symptoms[3]	4166				
Yes		**1.2 (1.1–1.4)**	**0.003**	1.1 (0.9–1.3)	0.2
No			Ref		
Smoking[4]	4142				
Yes		**2.1 (1.8–2.4)**	**<0.0001**	**1.4 (1.2–1.7)**	**0.0008**
No			Ref		
Second-hand smoke[4]	4163				
Never			Ref		
Some days		**1.4 (1.2–1.7)**	**<0.0001**	1.1 (0.9–1.3)	0.4
Every day		**1.9 (1.4–2.6)**	**0.001**	1.2 (0.8–1.7)	0.4
Recent antibiotic use[4]	4104				
Yes		**0.5 (0.4–0.7)**	**<0.0001**	**0.4 (0.3–0.7)**	**<0.0001**
No			Ref		
Attend bars, clubs, parties	4177				
<1/week or never			Ref		
1/week		**2.1 (1.7–2.5)**	**<0.0001**	**2.0 (1.6–2.5)**	**<0.0001**
2–3/week		**3.1 (2.6–3.7)**	**<0.0001**	**2.8 (2.2–3.6)**	**<0.0001**

		Bivariate analysis[1]		Multivariable analysis (N=2723)	
	N	**Prevalence Ratio (95% CI)[2]**	**p-value**	**Prevalence Ratio (95% CI)[2]**	**p-value**
≥4/week		**3.1 (2.2–4.4s)**	**0.0003**	**2.7 (1.6–4.4)**	**0.01**
Received MenACWY vaccine	3431				
Yes		1.0 (0.7–1.3)	0.8	--	--
No			Ref		
Received MenB vaccine doses[5]	3732				
0 doses			Ref		
1 dose MenB-FHbp		1.1 (0.9–1.3)	0.2	1.0 (0.8–1.4)	0.8
2 doses MenB-FHbp		1.2 (1.0–1.5)	0.07	1.2 (0.9–1.6)	0.2
3 doses MenB-FHbp		1.5 (1.0–2.3)	0.1	1.3 (0.7–2.2)	0.4
1 dose MenB-4C		0.9 (0.5–1.7)	0.7	0.9 (0.4–1.9)	0.7
2 doses MenB-4C		**2.0 (1.4–2.7)**	**0.002**	1.5 (1.0–2.3)	0.08

Bivariate and multivariable analysis was conducted using Poisson regression with generalized estimating equations (GEE) to account for individuals participating in multiple rounds.

[1] See table 1 for N included for each variable

[2] Prevalence ratios account for repeat participants using generalized estimating equation methods

[3] In the past 30 days

[4] In the past 2 weeks

[5] Includes only vaccine doses received ≥2 weeks before specimen collection

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Table 5

Bivariate and multivariable associations with carriage of *N. meningitidis* identified as serogroup B by real-time PCR among carriage evaluation participants at an Oregon university, March 2015–February 2016

	Bivariate analysis[1]		Multivariable analysis (N=2791)	
	Prevalence Ratio (95% CI)[2]	**p-value**	**Prevalence Ratio (95% CI)[1]**	**p-value**
Round				
1	Ref			
2	**1.8 (1.0–3.2)**	**0.04**	2.8 (1.0–7.6)	0.07
3	1.7 (0.9–3.1)	0.1	2.6 (1.1–6.2)	0.05
4	1.9 (1.0–3.7)	0.05	2.8 (1.0–7.6)	0.07
Gender				
Female	Ref			
Male	1.0 (0.6–1.6)	0.9	--	--
Year in school				
Freshman	Ref			
Sophomore	1.6 (0.9–2.8)	0.09	--	--
Junior	0.9 (0.5–1.8)	0.8	--	--
Senior	1.3 (0.7–2.3)	0.4	--	--
Age				
18	Ref			
19	**2.1 (1.0–4.2)**	**0.03**	2.0 (0.9–4.6)	0.09
20	**2.2 (1.0–4.8)**	**0.048**	2.2 (0.9–5.6)	0.1
21	1.4 (0.5–3.3)	0.5	0.9 (0.3–3.0)	0.9
22	**2.7 (1.2–6.3)**	**0.03**	2.6 (0.9–7.4)	0.1
Live on- vs. off-campus				
On-campus	Ref			
Off-campus	1.2 (0.8–1.9)	0.4	--	--
Type of residence				
Residence hall	Ref			

	Bivariate analysis[1]		Multivariable analysis (N=2791)	
	Prevalence Ratio (95% CI)[2]	**p-value**	**Prevalence Ratio (95% CI)[1]**	**p-value**
Apartment/house	1.4 (0.8–2.2)	0.2	--	--
Sorority/fraternity	2.0 (0.8–5.2)	0.2	--	--
Roommates				
0	Ref			
1	1.9 (0.8–4.8)	0.09	1.3 (0.5–3.7)	0.6
2	2.4 (0.8–6.6)	0.1	0.7 (0.2–2.7)	0.7
3+	**3.0 (1.2–7.4)**	**0.006**	1.5 (0.5–4.1)	0.4
Recent upper respiratory symptoms[3]				
Yes	1.1 (0.7–1.7)	0.7	--	--
No	Ref			
Smoking[4]				
Yes	**2.5 (1.6–3.9)**	**0.0003**	**2.0 (1.1–3.6)**	**0.02**
No	Ref			
Second-hand smoke[4]				
Never	Ref			
Some days	1.3 (0.8–2.0)	0.3	--	--
Every day	1.6 (0.6–4.1)	0.5	--	--
Recent antibiotic use[4]				
Yes	0.8 (0.3–2.0)	0.6	--	--
No	Ref			
Attend bars, clubs, parties				
<1/week or never	Ref			
1/week	1.5 (0.9–2.6)	0.2	1.3 (0.7–2.4)	0.5
2–3/week	**2.7 (1.6–4.6)**	**0.005**	**2.3 (1.1–4.6)**	**0.04**
≥4/week	3.2 (1.2–8.7)	0.2	3.0 (0.9–9.7)	0.2
Received MenACWY vaccine				
Yes	0.8 (0.4–1.3)	0.4	--	--

	Bivariate analysis[1]		Multivariable analysis (N=2791)	
	Prevalence Ratio (95% CI)[2]	**p-value**	**Prevalence Ratio (95% CI)[1]**	**p-value**
No	Ref			
Received MenB vaccine doses[5]				
0 doses	Ref			
1 dose MenB-FHbp	0.8 (0.5–1.4)	0.5	0.5 (0.2–1.0)	0.07
2 doses MenB-FHbp	1.3 (0.7–2.3)	0.5	0.7 (0.3–1.6)	0.4
3 doses MenB-FHbp	1.9 (0.5–7.2)	0.5	1.3 (0.3–5.4)	0.7
1 dose MenB-4C	0.7 (0.1–4.8)	0.7	0.6 (0.1–4.2)	0.5
2 doses MenB-4C	1.3 (0.4–4.3)	0.7	0.8 (0.2–2.6)	0.7

Bivariate and multivariable analysis was conducted using Poisson regression with generalized estimating equations (GEE) to account for individuals participating in multiple rounds.

[1] See Table 1 for N included for each variable.

[2] Prevalence ratios account for repeat participants using generalized estimating equation methods.

[3] In the past 30 days.

[4] In the past 2 weeks.

[5] Includes only vaccine doses received ≥2 weeks before specimen collection.

Table 6

Loss and acquisition of carried *N. meningitidis* among carriage evaluation participants at an Oregon university who participated in >= 2 carriage evaluation rounds during March 2015–February 2016, by vaccination status[1]

MenB vaccine doses[2]	N	Remained non-carriers N (%)	Lost carriage N (%)	Remained carriers N (%)	Acquired carriage N (%)
0	18	18 (100)	0 (0)	0 (0)	0 (0)
1 dose MenB-FHbp	234	197 (84)	4 (1.7)	17 (7.3)	16 (6.8)
2 doses MenB-FHbp	113	96 (85)	3 (2.7)	7 (6.2)	7 (6.2)
3 doses MenB-FHbp	20	17 (85)	0 (0)	2 (10)	1 (5.0)
1 dose MenB-4C	2	2 (100)	0 (0)	0 (0)	0 (0)
2 doses MenB-4C	9	6 (67)	0 (0)	2 (22)	1 (11)

[1] Individuals who participated in three rounds appear in the table twice: once for the interval from the first to the second round in which they participated and a second time for the interval from the second to the third round in which they participated. Individuals who participated in all four rounds appear in the table three times, once for the interval between rounds 1 and 2, once for rounds 2–3, and once for rounds 3–4.

[2] Includes only vaccine doses received ≥2 weeks before collection of second specimen.

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