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

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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 swab specimens and completed questionnaires during 4 carriage surveys over 11 months. Isolates were tested by real-time polymerase chain reaction analysis, slide agglutination, and whole-genome sequencing. Vaccination history was verified via university records and the state immunization registry.

Results. A total of 4225 oropharyngeal swab specimens from 3802 unique participants were analyzed. 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.

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; MenB-4C; MenB-FHbp.

In January–May 2015, 6 cases of serogroup B meningococcal disease, including 1 death, occurred among undergraduate students at a large Oregon university (undergraduate enrollment, approximately 20 000 students). One additional, nonfatal 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 32 (ST-32). In response to the outbreak, local public health officials provided the serogroup B meningococcal (MenB) vaccine MenB-4C (Bexsero, GlaxoSmithKline; 2-dose series) to a small number of interested students beginning in February 2015. Subsequently, mass vaccination campaigns with MenB-FHbp (Trumenba, Pfizer; 3-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 period and during freshmen orientation (June–August 2015). At least 25% of undergraduate students received at least 1 dose of MenB-FHbp or MenB-4C at the mass vaccination clinics (Fisher et al, unpublished data); however, owing 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 cases 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

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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 United States in 2014–2015 as a 2-dose (MenB-4C) or 2–3-dose (MenB-FHbp) series for persons aged 10–25 years [6]. Because these vaccines contain meningococcal outer membrane proteins present in both serogroup B and non–serogroup B meningococci, they could potentially affect carriage of all meningococci, not just serogroup B. However, only 2 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 affect meningococcal carriage and transmission and 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 a public health evaluation, rather than human subjects research, by the Centers for Disease Control and Prevention and the 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 campaigns at 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 (ie, 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 postvaccination waiting period and at high-traffic sites on the university campus. Participants provided informed consent and completed a short questionnaire assessing demographic characteristics, 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). Swabs were immediately plated on modified Thayer-Martin agar (BD BBL) 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) and tested by Gram stain (BD BBL); an oxidase test (Hardy Diagnostics; Santa Maria, CA) was performed on subcultured colonies of all gram-negative diplococci from the blood agar plate. When oxidase-positive, gram-negative diplococci were found, an API NH strip (bioMerieux; Durham, NC) and real-time polymerase chain reaction (PCR) for detection of *sodC* were used to confirm species [9]; discrepancies between test results were resolved through whole-genome sequencing. Remaining colonies were subcultured and further characterized by slide agglutination (SASG) with commercially available antisera (Difco; BD BBL), to detect expression of the serogroup A, B, C, W, X, and Y capsule antigens [10], and by singleplex real-time PCR analysis, to detect serogroup A, B, C, W, X, and Y capsule biosynthesis genes [10, 11]. Isolates were classified as nongroupable by real-time PCR analysis if the capsule biosynthesis genes for these 6 serogroups were not detected. Isolates negative for serogroup A, B, C, W, X, and Y capsule antigen expression by SASG were classified as "other" because these isolates could either be phenotypically nongroupable or express the non–disease-associated serogroup E or Z capsule antigens.

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

Table 1. Characteristics of Students at an Oregon University Who Participated in a Meningococcal Carriage Evaluation, March 2015–February 2016

Characteristic[a]	Round 1: March 2015	Round 2: May 2015	Round 3: October 2015	Round 4: February 2016	Total
Male sex	503/1138 (44)	426/1045 (41)	404/1025 (39)	358/923 (39)	**1691/4131 (41)**
Student standing					
Undergraduate					
Freshman	281/1141 (25)	295/1064 (28)	420/1035 (41)	409/922 (44)	**1406/4163 (34)**
Sophomore	271/1141 (24)	246/1064 (23)	206/1035 (20)	142/922 (15)	**865/4163 (21)**
Junior	283/1141 (25)	252/1064 (24)	181/1035 (17)	147/922 (16)	**863/4163 (21)**
Senior	303/1141 (27)	263/1064 (25)	212/1035 (20)	184/922 (20)	**962/4163 (23)**
Graduate student	3/1141 (0.3)	8/1064 (0.8)	16/1035 (1.6)	40/922 (4.3)	**67/4163 (1.6)**
Age, y					
18	146/1157 (13)	103/1062 (9.7)	374/1044 (36)	240/931 (26)	**863/4194 (21)**
19	275/1157 (24)	292/1062 (28)	210/1044 (20)	250/931 (27)	**1027/4194 (43)**
20	256/1157 (22)	221/1062 (21)	160/1044 (15)	122/931 (13)	**759/4194 (18)**
21	222/1157 (19)	192/1062 (18)	145/1044 (14)	124/931 (13)	**683/4194 (16)**
22	135/1157 (12)	149/1062 (14)	61/1044 (5.8)	74/931 (8.0)	**419/4194 (10)**
23–29	104/1157 (9.0)	95/1062 (9.0)	77/1044 (7.4)	102/931 (11)	**378/4194 (9.0)**
≥30	19/1157 (1.6)	10/1062 (0.9)	17/1044 (1.6)	19/931 (2.0)	**65/4194 (1.5)**
On-campus residence	273/1002 (27)	326/1047 (31)	427/1018 (42)	411/894 (46)	**1437/3961 (36)**
Residence type					
Residence hall	279/912 (31)	312/1032 (30)	410/988 (42)	397/877 (45)	**1398/3809 (37)**
Apartment/house	590/912 (65)	662/1032 (64)	561/988 (57)	454/877 (52)	**2267/3809 (60)**
Sorority/fraternity	43/912 (4.7)	58/1032 (5.6)	17/988 (1.7)	26/877 (3.0)	**144/3809 (3.8)**
Roommates, no.[b]					
0	89/892 (10)	126/1027 (12)	75/990 (7.6)	68/856 (7.9)	**358/3765 (9.5)**
1	346/892 (39)	407/1027 (40)	515/990 (52)	477/856 (56)	**1745/3765 (46)**
2	134/892 (15)	136/1027 (13)	123/990 (12)	93/856 (11)	**486/3765 (13)**
≥3	266/892 (30)	309/1027 (30)	221/990 (22)	177/856 (21)	**973/3765 (26)**
Live with family	57/892 (6.4)	49/1027 (4.8)	56/990 (5.7)	41/856 (4.8)	**203/3765 (5.4)**
Recent upper respiratory tract symptoms[c]	527/1156 (46)	324/1050 (31)	348/1029 (34)	361/931 (39)	**1560/4166 (37)**
Recent smoking[d]	396/1135 (35)	326/1058 (31)	339/1033 (33)	305/916 (33)	**1366/4142 (33)**
Recent secondhand smoke exposure[d]					
Never	531/1161 (46)	470/145 (45)	472/1031 (46)	456/926 (49)	**1929/4163 (46)**
Some days	564/1161 (49)	541/1045 (52)	513/1031 (50)	451/926 (49)	**2069/4163 (50)**
Every day	66/1161 (5.7)	34/1045 (3.3)	46/1031 (4.5)	19/926 (2.1)	**165/4163 (4.0)**
Recent antibiotic use[d]	134/1136 (12)	74/1036 (7.1)	91/1022 (8.9)	84/910 (9.2)	**383/4104 (9.2)**
Attend bars, clubs, or parties, times/wk					
<1 or never	574/1165 (49)	548/1056 (52)	610/1035 (59)	536/921 (58)	**2268/4177 (54)**
1	315/1165 (27)	292/1056 (28)	276/1035 (27)	235/921 (26)	**1118/4177 (27)**
2–3	242/1165 (21)	193/1056 (18)	130/1035 (13)	137/921 (15)	**702/4177 (17)**
≥4	34/1165 (2.9)	23/1056 (2.2)	19/1035 (1.8)	13/921 (1.4)	**89/4177 (2.1)**
Received MenACWY vaccine	809/972 (83)	736/876 (84)	683/841 (81)	592/742 (80)	**2820/3431 (82)**
MenB vaccine dose(s) received, by vaccine, no.[e]					
0	1006/1011 (100)	40/872 (4.6)	349/992 (35)	223/857 (26)	**1618/3732 (43)**
MenB-FHbp					
1	1/1011 (0.1)	756/872 (87)	277/992 (28)	221/857 (26)	**1255/3732 (34)**
2	2/1011 (0.2)	10/872 (1.2)	291/992 (29)	296/857 (35)	**599/3732 (16)**
3	0/1011 (0)	0/872 (0)	11/992 (1.1)	53/857 (6.2)	**64/3732 (1.7)**
MenB-4C					
1	2/1011 (0.2)	17/872 (2.0)	21/992 (2.1)	21/857 (2.5)	**61/3732 (1.6)**
2	0/1011 (0)	49/872 (5.6)	43/992 (4.3)	43/857 (5.0)	**135/3732 (3.6)**

Data are no. of students with the characteristic/no. evaluated (%).

[a]Participants with missing data are not shown.

[b]Unless otherwise indicated, data are for students who are not living with family.

[c]In the past 30 d.

[d]In the past 2 wk.

[e]Data reflect vaccine doses received ≥2 wk before specimen collection.

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 statistical analyses of patient characteristics and calculated prevalence ratios 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 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 (ie, those with a *P* value of <.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 before 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 4526 participants were enrolled over 4 carriage evaluation rounds. Of these, 301 were excluded: 14 were excluded because of ineligibility; 284 were excluded because their swab could not be tested owing to laboratory equipment failure (n = 265), plating error, or contamination or because it was missing; and 3 were excluded because consent forms or questionnaires were missing. This left 4225 oropharyngeal swabs from **3509** unique participants for analysis. A total of **613** students participated in >1 evaluation round: **518** participated in 2 rounds, **91** participated in 3 rounds, and 4 participated in 4 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 of 4225 participants (81%), and MenB vaccination status could be assigned for 3732 of 4225 (88%; Table 1). MenACWY vaccination status was validated from written records for 2854 of 4225 participants (68%), and MenB vaccination status was validated for 3063 of 4225 (72%); remaining participants had vaccination status assigned on the basis of 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 ≥1 dose of a MenB vaccine ≥14 days before participating in carriage evaluation (Table 1). Inclusion of individuals with documented and those with self-reported vaccination status revealed that 64 (1.7%; all unique participants) received a complete 3-dose series of MenB-FHbp and that 135 (3.6%; 133 unique participants) received a complete 2-dose series of MenB-4C (Table 1).

Table 2. Overall and Serogroup-Specific Meningococcal Carriage Among Students at an Oregon University Who Participated in a Carriage Evaluation, March 2015–February 2016

Variable	Round 1: March 2015, Students, No. (%) (n = 1173)	Round 2: May 2015, Students, No. (%) (n = 1069)	Round 3: October 2015, Students, No. (%) (n = 1045)	Round 4: February 2016, Students, No. (%) (n = 938)	Total Students, No. (%) (n = 4225)
N. meningitidis carriage	167 (14)	183 (17)	110 (11)	163 (17)	**622 (15)**
Serogroup[a]					
Genotypic analysis (by real-time PCR)					
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 analysis (by SASG)					
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)**

Abbreviation: *N. meningitidis*, *Neisseria meningitidis*.

[a]Real-time polymerase chain reaction (PCR) analysis and slide agglutination (SASG) analysis both tested for serogroups A, B, C, W, X, and Y. For SASG analysis, 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 real-time PCR analysis, isolates were classified as nongroupable if serogroup A, B, C, W, X, and Y biosynthesis genes were not detected.

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 analysis) and were genotypically (by real-time PCR analysis) 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 prevalence of serogroups C, W, X, and Y was determined to be <1% by real-time PCR analysis and <0.5% by SASG analysis (Table 2).

Multilocus ST could be assessed through whole-genome sequencing for 78 of 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 ST (n = 27) (Table 3).

In bivariate analyses, increased carriage of any *N. meningitidis* was associated with participation during rounds 2 or 4; male sex; 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 secondhand smoke exposure; and attending parties, bars, clubs, or other social mixing events ≥1 time 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 ≥1 time per week remained associated with increased carriage, and recent antibiotic use remained associated with decreased carriage (Table 4).

Receipt of 2 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 of 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).

Table 3. Phenotypic Serogroup Determination, Clonal Complex, and Sequence Type of 78 Carried Neisseria meningitidis Isolates Identified as Serogroup B by Real-Time Polymerase Chain Reaction That Were Recovered From Students at an Oregon University Who Participated in a Carriage Evaluation, March 2015–February 2016

Isolates, No.[a]	Phenotypic Serogroup (by SASG)	CC	ST
1	NG	CC1117	11855
1	NG	CC1157	1157
2	B	CC162	162
1	NG	CC162	2153
1	B	CC174	1466
2	B	CC213	213
5	NG	CC213	213
1	B	CC213	3496
1	NG	CC213	11852
1	NG	CC269	3091
1	B	CC32/ET-5	322
1	NG	CC32/ET-5	322
1	B	CC32/ET-5	8758
2	NG	CC32/ET-5[b]	11395
3	NG	CC35	35
2	NG	CC35	11392
5	NG	CC41/44/Lineage 3	44
5	B	CC41/44/Lineage 3	136
22	NG	CC41/44/Lineage 3	136
6	NG	CC41/44/Lineage 3	409
1	NG	CC41/44/Lineage 3	1097
1	B	CC41/44/Lineage 3	1489
1	NG	CC41/44/Lineage 3	5881
1	NG	CC461	1946
1	NG	CC461	11861
2	NG	CC4821	11858
1	NG	CC53	53
2	NG	CC865	865
1	NG	Unassigned	8537
1	B	Unassigned	9069
1	NG	Unassigned	11294
1	B	Unassigned	11860

Abbreviations: CC, clonal complex; SASG, slide agglutination; ST, sequence type.

[a]One isolate (genotypically serogroup B, phenotypically NG) was excluded because the CC and ST could not be determined.

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

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 **42** individuals in the longitudinal analysis had not received any MenB vaccine doses by their second round of participation (Table 6). **Four** of these **42** individuals carried *N. meningitidis* during **both their first and second rounds** of participation; **none of the 42 gained or lost carriage between participation rounds** (Table 6). **Given these small numbers**, carriage loss among vaccinated and

Table 4. Bivariate and Multivariable Associations With Carriage of Any *Neisseria meningitidis* Among Students at an Oregon University Who Participated in a Carriage Evaluation, March 2015–February 2016

		Bivariate Analysis		Multivariable Analysis (n = 2723)	
Variable	Students, No.	Prevalence Ratio (95% CI)[a]	*P*	Prevalence Ratio (95% CI)[a]	*P*
Round	4225				
1	…	Reference		Reference	
2	…	**1.2 (1.1–1.5)**	**.01**	1.0 (.7–1.5)	.9
3	…	0.8 (.7–1.0)	.08	0.8 (.6–1.1)	.1
4	…	**1.2 (1.0–1.5)**	**.02**	1.2 (.8–1.7)	.3
Sex	4131				
Female	…	Reference		Reference	
Male	…	**1.5 (1.3–1.7)**	**<.0001**	**1.2 (1.0–1.5)**	**.03**
Student standing	4163				
Freshman	…	Reference		Reference	
Sophomore	…	**1.4 (1.2–1.7)**	**.0008**	0.8 (.6–1.1)	.2
Junior	…	**1.3 (1.0–1.5)**	**.03**	0.7 (.5–1.1)	.2
Senior	…	1.2 (.9–1.4)	.2	0.8 (.5–1.4)	.5
Age, y	4194				
18	…	Reference		Reference	
19	…	**1.5 (1.2–1.9)**	**.0004**	1.2 (.9–1.6)	.3
20	…	**1.8 (1.4–2.2)**	**<.0001**	**1.6 (1.1–2.3)**	**.02**
21	…	**1.4 (1.1–1.8)**	**.006**	1.1 (.7–1.8)	.7
22	…	**1.4 (1.0–1.8)**	**.04**	0.8 (.5–1.5)	.6
23–29	…	0.8 (.5–1.1)	.2	0.8 (.4–1.5)	.5
≥30	…	0.8 (.3–1.9)	.6	1.8 (.7–5.2)	.4
On- vs off-campus residence	3961				
On campus	…	Reference		Reference	
Off campus	…	**1.2 (1.1–1.5)**	**.0008**	1.3 (.7–2.2)	.4
Residence type	3809				
Residence hall	…	Reference		Reference	
Apartment/house	…	**1.2 (1.0–1.4)**	**.02**	0.9 (.5–1.8)	.8
Sorority/fraternity	…	**2.5 (1.9–3.3)**	**<.0001**	1.3 (.7–2.4)	.4
Roommates, no.[b]	3765				
0	…	Reference		Reference	
1	…	1.0 (.7–1.3)	.8	1.0 (.7–1.4)	1.0
2	…	1.3 (.9–1.7)	.2	1.0 (.7–1.5)	1.0
≥3	…	**1.5 (1.1–2.0)**	**.003**	1.2 (.8–1.7)	.3
Live with family	…	**0.4 (.2–.7)**	**.0005**	0.6 (.3–1.4)	.2
Recent upper respiratory tract symptoms[c]	4166				
Yes	…	**1.2 (1.1–1.4)**	**.003**	1.1 (.9–1.3)	.2
No	…	Reference		Reference	
Recent smoking[d]	4142				
Yes	…	**2.1 (1.8–2.4)**	**<.0001**	**1.4 (1.2–1.7)**	**.0008**
No	…	Reference		Reference	
Recent secondhand smoke exposure[d]	4163				
Never	…	Reference		Reference	
Some days	…	**1.4 (1.2–1.7)**	**<.0001**	1.1 (.9–1.3)	.4
Every day	…	**1.9 (1.4–2.6)**	**.001**	1.2 (.8–1.7)	.4
Recent antibiotic use[d]	4104				
Yes	…	**0.5 (.4–.7)**	**<.0001**	**0.4 (.3–.7)**	**<.0001**
No	…	Reference		Reference	
Attend bars, clubs, or parties, times/wk	4177				
<1 or never	…	Reference		Reference	
1	…	**2.1 (1.7–2.5)**	**<.0001**	**2.0 (1.6–2.5)**	**<.0001**
2–3	…	**3.1 (2.6–3.7)**	**<.0001**	**2.8 (2.2–3.6)**	**<.0001**
≥4	…	**3.1 (2.2–4.4s)**	**.0003**	**2.7 (1.6–4.4)**	**.01**

Table 4. Continued

Variable	Bivariate Analysis			Multivariable Analysis (n = 2723)	
	Students, No.	Prevalence Ratio (95% CI)[a]	*P*	Prevalence Ratio (95% CI)[a]	*P*
Received MenACWY vaccine	3431				
Yes	…	1.0 (.7–1.3)	.8	…	
No	…	Reference		…	
MenB vaccine dose(s) received, by vaccine, no.[e]	3732				
0	…	Reference		Reference	
MenB-FHbp					
1	…	1.1 (.9–1.3)	.2	1.0 (.8–1.4)	.8
2	…	1.2 (1.0–1.5)	.07	1.2 (.9–1.6)	.2
3	…	1.5 (1.0–2.3)	.1	1.3 (.7–2.2)	.4
MenB-4C					
1	…	0.9 (.5–1.7)	.7	0.9 (.4–1.9)	.7
2	…	**2.0 (1.4–2.7)**	**.002**	1.5 (1.0–2.3)	.08

Bivariate and multivariable analyses were conducted using Poisson regression with generalized estimating equations to account for individuals participating in multiple rounds.

Abbreviation: CI, confidence interval.

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

[b]Unless otherwise indicated, data are for students who are not living with family.

[c]In the past 30 d.

[d]In the past 2 wk.

[e]Data reflect vaccine doses received ≥2 wk before specimen collection.

unvaccinated individuals could not be compared. Meningococcal carriage acquisition was observed in 5%–**20%** 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, owing to small numbers. **Five** individuals acquired genotypically serogroup B (phenotypically nongroupable) meningococci **while one individual acquired meningococci that were genotypically and phenotypically serogroup Y**; all other individuals with new carriage acquired genotypically nongroupable meningococci.

DISCUSSION

The 4 meningococcal carriage evaluation rounds spanned 11 months, beginning in the middle of the outbreak and ending 9 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, the prevalence of carriage had increased above the baseline prevalence in round 1. In the multivariable analysis, differences in carriage prevalence 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, the 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 3 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. A low prevalence of 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

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[a]		Multivariable Analysis (n = 2791)	
Variable	Prevalence Ratio (95% CI)[b]	*P*	Prevalence Ratio (95% CI)[b]	*P*
Round				
1	Reference		Reference	
2	**1.8 (1.0–3.2)**	**.04**	2.8 (1.0–7.6)	.07
3	1.7 (.9–3.1)	.1	2.6 (1.1–6.2)	.05
4	1.9 (1.0–3.7)	.05	2.8 (1.0–7.6)	.07
Sex				
Female	Reference		…	
Male	1.0 (.6–1.6)	.9	…	
Student status				
Freshman	Reference		…	
Sophomore	1.6 (.9–2.8)	.09	…	
Junior	0.9 (.5–1.8)	.8	…	
Senior	1.3 (.7–2.3)	.4	…	
Age, y				
18	Reference		Reference	
19	**2.1 (1.0–4.2)**	**.03**	2.0 (.9–4.6)	.09
20	**2.2 (1.0–4.8)**	**.048**	2.2 (.9–5.6)	.1
21	1.4 (.5–3.3)	.5	0.9 (.3–3.0)	.9
22	**2.7 (1.2–6.3)**	**.03**	2.6 (.9–7.4)	.1
On- vs. off-campus residence				
On campus	Reference		…	
Off campus	1.2 (.8–1.9)	.4	…	
Residence type				
Residence hall	Reference		…	
Apartment/house	1.4 (.8–2.2)	.2	…	
Sorority/fraternity	2.0 (.8–5.2)	.2	…	
Roommates, no.[c]				
0	Reference		Reference	
1	1.9 (.8–4.8)	.09	1.3 (.5–3.7)	.6
2	2.4 (.8–6.6)	.1	0.7 (.2–2.7)	.7
≥3	**3.0 (1.2–7.4)**	**.006**	1.5 (.5–4.1)	.4
Recent upper respiratory tract symptoms[d]				
Yes	1.1 (.7–1.7)	.7	…	
No	Reference		…	
Recent smoking[e]				
Yes	**2.5 (1.6–3.9)**	**.0003**	**2.0 (1.1–3.6)**	**.02**
No	Reference		Reference	
Recent secondhand smoke exposure[e]				
Never	Reference		…	
Some days	1.3 (.8–2.0)	.3	…	
Every day	1.6 (.6–4.1)	.5	…	
Recent antibiotic use[e]				
Yes	0.8 (.3–2.0)	.6	…	
No	Reference		…	
Attend bars, clubs, or parties, times/wk				
<1 or never	Reference		Reference	
1	1.5 (.9–2.6)	.2	1.3 (.7–2.4)	.5
2–3	**2.7 (1.6–4.6)**	**.005**	**2.3 (1.1–4.6)**	**.04**
≥4	3.2 (1.2–8.7)	.2	3.0 (.9–9.7)	.2
Received MenACWY vaccine				
Yes	0.8 (.4–1.3)	.4	…	
No	Reference		…	

Table 5. Continued

Variable	Bivariate Analysis[a]		Multivariable Analysis (n = 2791)	
	Prevalence Ratio (95% CI)[b]	*P*	Prevalence Ratio (95% CI)[b]	*P*
MenB vaccine dose(s) received, by vaccine, no.[f]				
0	Reference		Reference	
MenB-FHbp				
1	0.8 (.5–1.4)	.5	0.5 (.2–1.0)	.07
2	1.3 (.7–2.3)	0.5	0.7 (.3–1.6)	.4
3	1.9 (.5–7.2)	0.5	1.3 (.3–5.4)	.7
MenB-4C				
1	0.7 (.1–4.8)	0.7	0.6 (.1–4.2)	.5
2	1.3 (.4–4.3)	0.7	0.8 (.2–2.6)	.7

Bivariate and multivariable analyses were conducted using Poisson regression with generalized estimating equations to account for individuals participating in multiple rounds.

Abbreviation: CI, confidence interval.

[a]See Table 1 for the no. of students included for each variable.

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

cUnless otherwise indicated, data are for students who are not living with family.

[d]In the past 30 d.

[e]In the past 2 wk.

[f]Data reflect vaccine doses received ≥2 wk before specimen collection.

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 a relatively high carriage prevalence 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 a 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, owing

Table 6. Loss and Acquisition of Carried Neisseria meningitidis Among Students at an Oregon University Who Participated in ≥2 Rounds of a Carriage Evaluation During March 2015–February 2016, by Vaccination Status

MenB Vaccine Dose(s) Received, by Vaccine, no.[a]	Overall, Students, No.	Remained Non-carriers, Students, No. (%)	Lost Carriage, Students, No. (%)	Remained Carriers, Students, No. (%)	Acquired Carriage, Students, No. (%)
0	**42**	**38 (90)**	0 (0)	**4 (10)**	0 (0)
MenB-FHbp					
1	**297**	**249** (84)	**7 (2.4)**	**20 (6.7)**	**21 (7.1)**
2	**287**	**249 (87)**	**8 (2.8)**	**16 (5.6)**	**14 (4.9)**
3	**30**	**24 (80)**	0 (0)	**3** (10)	**3 (10)**
MenB-4C					
1	**5**	**4 (80)**	0 (0)	0 (0)	**1 (20)**
2	**18**	**13 (72)**	0 (0)	**3 (17)**	**2 (11)**

Individuals who participated in 3 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 4 rounds appear in the table 3 times, once for the interval between rounds 1 and 2, once for rounds 2–3, and once for rounds 3–4.

[a]Data reflect vaccine doses received ≥2 wk before collection of the second specimen.

to the extremely low carriage prevalence 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 differ substantially with regard to characteristics that may affect the 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 for close contacts of patients with meningococcal disease 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.

Notes

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