

Meningococcal Carriage Evaluation in Response to a Serogroup B Meningococcal Disease Outbreak and Mass Vaccination Campaign at a University — Oregon, 2015–2016

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Background

- Two vaccines for serogroup B meningococcal disease (MenB vaccines) licensed in the US in 2014–2015: MenB-FHbp (Trumenba[®], Pfizer) and MenB-4C (Bexsero[®], GlaxoSmithKline)
- Licensed based on immunogenicity and safety data suggesting they help protect vaccinated individuals from meningococcal disease
- Impact of these vaccines on asymptomatic meningococcal carriage and herd protection is unknown**

Meningococcal Disease

- Caused by Gram-negative diplococcus *Neisseria meningitidis*
- 10–15% case-fatality ratio; 11–19% of survivors have long-term sequelae
- Classified into serogroups based on polysaccharide capsule
 - A, B, C, W, X, Y are primary causes of disease
 - Nongroupable bacteria lack capsule and rarely cause disease
 - Serogroup B is most common cause of meningococcal disease in adolescents in the US**

Meningococcal vaccines

- The meningococcal conjugate vaccine (MenACWY) routinely recommended for adolescents protects against serogroups A, C, W, and Y, but not serogroup B
- Serogroup B vaccines are based on outer membrane proteins
 - Multiple alleles and variable expression, so MenB vaccines not protective against all serogroup B strains
 - Not serogroup-specific: could protect against other serogroups and nongroupable meningococcal bacteria

Asymptomatic nasopharyngeal meningococcal carriage

- Asymptomatic nasopharyngeal carriage is >100x more common than disease
- Lasts weeks to months and can last a year or more^{1,2}
- Carriage and disease are distinct outcomes of acquisition
 - Likelihood of establishing carriage vs. invasive disease varies by strain

Meningococcal transmission

- Spread through close contact
- Respiratory or oral secretions from patients or asymptomatic carriers
- Risk factors include social mixing,^{3,4} age,^{5,6} and smoking⁵

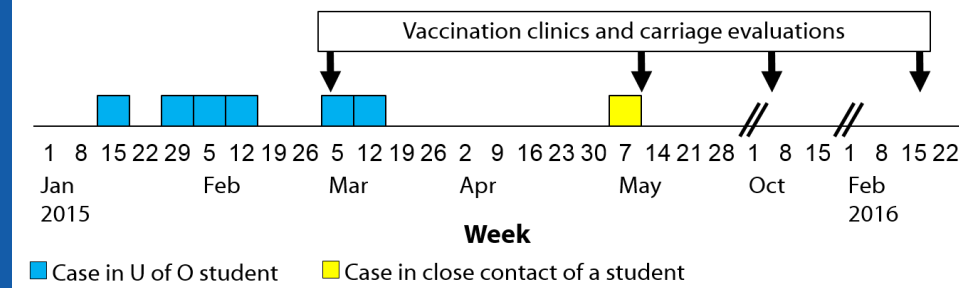
Meningococcal Vaccine Impact on Meningococcal Carriage

- MenC vaccines: Reduced serogroup C carriage in UK by 66%⁷
- MenA (PsA-TT): Dramatically reduced serogroup A carriage in Burkina Faso⁸
- Limited data on MenB vaccine impact on carriage
 - MenB-4C: 18% (95% CI: 3–31%) reduction in carriage of any meningococcal bacteria
 - No impact on serogroup B carriage⁹
 - No published data on MenB-FHbp impact on carriage

Context

- Outbreak of 7 serogroup B cases at an Oregon university in January–May, 2015
 - 1 death
 - All cases caused by same strain of sequence type (ST) 32
- Bexsero[®] provided to limited number of students beginning in February, 2015
- Mass vaccination clinics with Trumenba[®]
 - Also available during freshman orientation and at local pharmacies
- ~52% of targeted students had received 1+ doses of MenB vaccine by March, 2016

Figure 1. Timeline of outbreak, vaccination clinics, and carriage evaluation



Methods

- Objectives:
 - Determine baseline carriage of *N. meningitidis* and the outbreak strain
 - Assess effect of MenB vaccination on overall and serogroup B carriage
- Eligibility: all students eligible to receive MenB vaccine at mass vaccination clinic (all undergraduates; graduate students living in undergraduate dormitories or with specific medical conditions)
- Recruited students during 4 evaluation rounds at mass vaccination clinics and high-traffic sites
- Participants completed brief questionnaire and provided oropharyngeal swab
- Samples were cultured and isolates tested via Gram stain, biochemical tests, real-time PCR, slide agglutination, and whole genome sequencing

Results

Table 1. MenB mass vaccination campaign coverage, carriage evaluation participants, and results

Carriage Evaluation Round	Month	Carriage evaluation participants (N)
1	March 2015	1173
2	May 2015	1069
3	October 2015	1045
4	February 2016	938
Total		4,225

Figure 2. MenB vaccine receipt among carriage evaluation participants

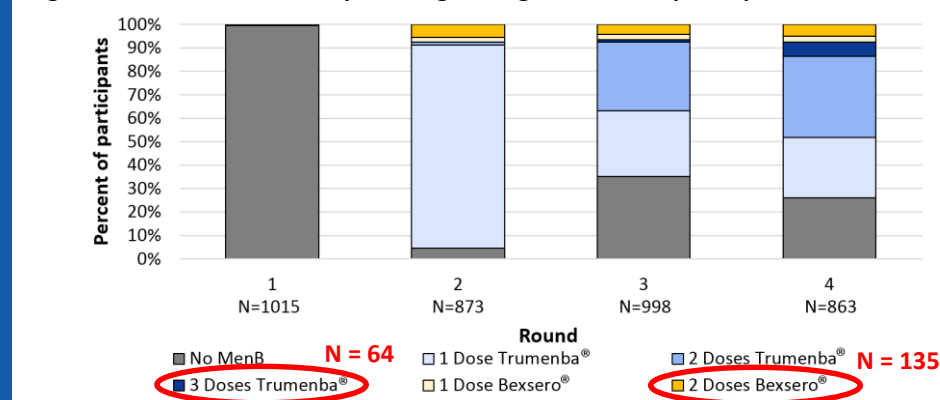
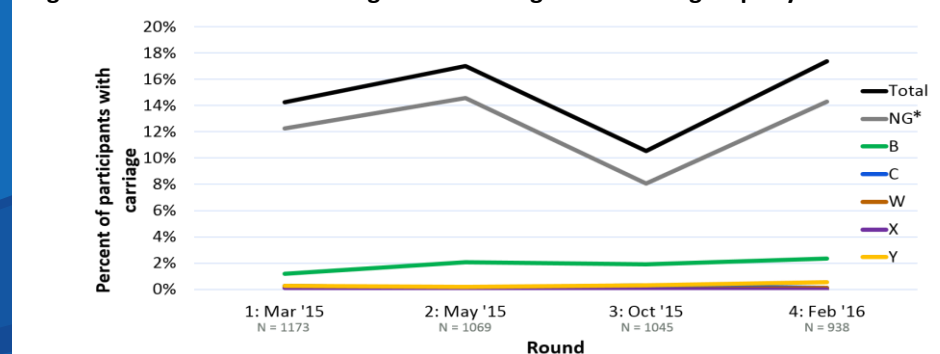


Figure 3. Distribution of meningococcal carriage isolate serogroups by real-time PCR



*Includes B isolates not tested by PCR because they were serogroup E by SASG

****No carriage of the outbreak strain detected during any round****

Table 2. Multivariable associations with carriage of any meningococcal bacteria (N=2723)

Characteristic	Prevalence Ratio ¹ (95% CI)	p-value
Gender (reference = female)		
Male	1.2 (1.0-1.5)	0.03
Age (reference = 18 years)		
19	1.2 (0.9-1.6)	0.3
20	1.6 (1.1-2.3)	0.02
21	1.1 (0.7-1.8)	0.8
22	0.8 (0.5-1.5)	0.6
23-29	0.8 (0.4-1.5)	0.5
30+	1.8 (0.7-5.2)	0.4
Smoking ²	1.4 (1.2-1.7)	0.0008
Recent antibiotic use ²	0.4 (0.3-0.7)	<0.0001
Attend bars, clubs, or parties (reference = <1/week or never)		
1/week	2.0 (1.6-2.5)	<0.0001
2-3/week	2.8 (2.2-3.6)	<0.0001
≥4/week	2.7 (1.6-4.4)	0.01
Received MenB vaccine doses ³ (reference = 0 doses)		
1 dose MenB-FHbp (Trumenba [®])	1.0 (0.8-1.4)	0.8
2 doses MenB-FHbp (Trumenba [®])	1.2 (0.9-1.6)	0.2
3 doses MenB-FHbp (Trumenba [®])	1.3 (0.7-2.2)	0.4
1 dose MenB-4C (Bexsero [®])	0.9 (0.4-1.9)	0.7
2 doses MenB-4C (Bexsero [®])	1.5 (1.0-2.3)	0.08

¹Prevalence ratios account for repeat participants using GEE methods of Poisson regression and are adjusted for non-statistically significant variables round; year in school; living on- vs. off-campus or in a residence hall, apartment/house, or sorority or fraternity; number of roommates; having recent upper respiratory tract infection symptoms; and second-hand smoking; ²In the past 30 days; ³Includes only vaccine doses received ≥2 weeks before specimen collection

Discussion

Summary

- In each round: 11–17% meningococcal carriage, 1–2% serogroup B carriage
 - Carriage prevalence similar in two other recent carriage evaluations at US universities (CDC unpublished data)
 - Higher than other recent US estimates of 1–8% among general population^{10,11}
- No carriers of outbreak strain identified
 - However**, we know strain was still circulating during round 1 – additional outbreak cases occurred through May 2015
- Male gender, age, smoking, social mixing associated with higher carriage
- Antibiotic use associated with lower carriage
- No association between MenB-FHbp or MenB-4C vaccination and carriage

Challenges

- Observational evaluation: potential for unidentified confounding
- Culturing oropharyngeal swab samples highly specific but sensitivity unknown
- Evaluation crossed 2 academic school years; summer vacation likely temporarily impacted transmission

Conclusions

- MenB-FHbp and MenB-4C do not have a rapid, large impact on meningococcal carriage** and therefore do not rapidly provide herd protection in the context of an outbreak
- Reinforces importance of high vaccination coverage during outbreaks and chemoprophylaxis for close contacts of meningococcal disease cases

****See Poster #721 for an additional evaluation of the impact of a serogroup B meningococcal vaccine on meningococcal carriage****

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