Persistence of serogroup C antibody responses following quadrivalent meningococcal conjugate vaccination in United States military personnel

Manisha Patel, Sandra Romero-Steiner, Michael P. Broderick, Cynthia G. Thomas, Brian D. Plikaytis, Daniel S. Schmidt, Scott E. Johnson, Andrea S. Milton, George M. Carline, Thomas A. Clark, Nancy E. Messonnier, Amanda C. Cohn, and Dennis J. Faix

A Meningitis and Vaccine-Preventable Diseases Branch, Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, MS C-25, Atlanta, GA 30333, USA

B Office of Science and Public Health Practice, Office of Public Health Preparedness and Response, Centers for Disease Control and Prevention, 1600 Clifton Road, MS D 44, Atlanta, GA 30333, USA

C Operational Infectious Diseases, Naval Health Research Center, 140 Sylvester Road, San Diego, CA 92106, USA

Abstract

Serogroup C meningococcal (MenC) disease accounts for one-third of all meningococcal cases and causes meningococcal outbreaks in the U.S. Quadrivalent meningococcal vaccine conjugated to diphtheria toxoid (MenACYW_D) was recommended in 2005 for adolescents and high risk groups such as military recruits. We evaluated anti-MenC antibody persistence in U.S. military personnel vaccinated with either MenACYW_D or meningococcal polysaccharide vaccine (MPSV4). Twelve hundred subjects vaccinated with MenACYW_D from 2006 to 2008 or MPSV4 from 2002 to 2004 were randomly selected from the Defense Medical Surveillance System. Baseline serologic responses to MenC were assessed in all subjects; 100 subjects per vaccine group were tested during one of the following six post-vaccination time-points: 5–7, 11–13, 17–19, 23–25, 29–31, or 35–37 months. Anti-MenC geometric mean titers (GMT) were measured by rabbit complement serum bactericidal assay (rSBA) and geometric mean concentrations (GMC) by enzyme-linked immunosorbent assay (ELISA). Continuous variables were compared using the Wilcoxon rank sum test and the proportion of subjects with an rSBA titer ≥8 by chi-square. Pre-vaccination rSBA GMT was <8 for the MenACYW_D group. rSBA GMT increased to 703 at 5–7 months post-vaccination and decreased by 94% to 43 at 3 years post-vaccination. GMT was
significantly lower in the MenACWY \textsubscript{D} group at 5–7 months post-vaccination compared to the MPSV4 group. The percentage of MenACWY \textsubscript{D} recipients achieving an rSBA titer of ≥8 decreased from 87% at 5–7 months to 54% at 3 years. There were no significant differences between vaccine groups in the proportion of subjects with a titer of ≥8 at any time-point. GMC for the MenACWY \textsubscript{D} group was 0.14 µg/mL at baseline, 1.07 µg/mL at 5–7 months, and 0.66 µg/mL at 3 years, and significantly lower than the MPSV4 group at all time-points. Anti-MenC responses wane following vaccination with MenACYW \textsubscript{D}; a booster dose is needed to maintain protective levels of circulating antibody.

Keywords
Meningococcal vaccine; Conjugate; Polysaccharide; Antibody persistence

1. Introduction

In the United States, serogroups B, C and Y \textit{Neisseria meningitidis} each account for approximately one-third of meningococcal cases [1]. From 1998 to 2007, serogroup C (MenC) disease resulted in the highest case fatality ratio (14.6) among the three serogroups [1]. MenC often results in more severe sequelae in its survivors and has a predilection to cause outbreaks [2–4]. Sequence type (ST) 11/electrophoretic type (ET) 37 clonal complex was responsible for outbreaks in U.S. army military recruits in the 1960s and continues to cause outbreaks in the U.S. today [1,5]. Although disease rates for all serogroups are at a historic low, morbidity and mortality among cases remains unchanged.

Prior to 2005, quadrivalent (A, C, Y, W) meningococcal polysaccharide vaccine, MPSV4 (\textit{Menomune\textsuperscript{®}}, Sanofi Pasteur, Swiftwater, PA, USA), was used routinely in U.S. military recruits to reduce the risk of disease during basic training. However, routine vaccination of the general population was not recommended because of its limited duration of protection. In 2005, the Advisory Committee on Immunization Practices (ACIP) recommended vaccination of adolescents and other persons at high risk for meningococcal disease with a newly licensed quadrivalent meningococcal conjugate vaccine (MenACYW) [6]. Two quadrivalent meningococcal conjugate vaccines are currently available for adolescents in the U.S. MenACWY \textsubscript{D} (\textit{Menactra\textsuperscript{®}}, diphtheria toxoid conjugate, Sanofi Pasteur, Swiftwater, PA, USA) was licensed in 2005 and MenACWY \textsubscript{CRM} (\textit{Menveo\textsuperscript{TM}}, CRM-197 conjugate, Novartis Vaccines, Cambridge, MA, USA) in 2010. The ACIP recommended use of either vaccine for adolescents aged 11–18 years and other persons at increased risk for meningococcal disease, including military recruits and first year college students living in residential housing. Upon licensure, quadrivalent meningococcal conjugate vaccines were expected to provide protection for at least 5–10 years. However, a limited number of persistence studies conducted during clinical trials suggest antibody waning occurs faster than previously predicted [7,8].

To address increasing concern for limited duration of protection following vaccination with meningococcal conjugate vaccine, in January 2011 the ACIP recommended a booster dose for adolescents on or after their 16th birthday to provide optimal protection throughout the
period of increased risk (16–21 years of age). Booster doses continue to be recommended every 5 years for high risk groups, such as those with certain immunologic disorders, as well as military personnel who continue to be at increased risk [9]. However, data supporting the optimal interval for vaccination of these high risk groups are limited. The objective of this study is to evaluate antibody persistence to MenC following vaccination with MenACWY\textsubscript{D} in military personnel to inform US public health policy for quadrivalent meningococcal vaccines. Serologic responses over a 3 year period are compared to military recruits who were routinely vaccinated with meningococcal polysaccharide vaccines (MPSV4) prior to licensure of conjugate vaccines.

2. Materials and methods

2.1. Study design and participants

We conducted a retrospective cohort study among U.S. military service personnel previously vaccinated with either quadrivalent meningococcal conjugate (MenACWY\textsubscript{D}) or polysaccharide (MPSV4) vaccine. Eligibility criteria included receipt of one dose of MPSV4 from 2002 to 2004 or MenACWY\textsubscript{D} from 2006 to 2008, availability of sera prior to vaccination, and at least one sample within 3 years post-vaccination. Individuals with a history of ≥2 doses of meningococcal vaccine were excluded. Subjects meeting the eligibility criteria were selected from the U.S. Department of Defense’s (DoD) Defense Medical Surveillance System (DMSS) electronic database. DMSS integrates medical surveillance data for over ten million individuals who have served in the U.S. military since 1990 [10,11]. Sera that had been previously collected and subsequently stored in the Department of Defense Serum Repository (DoDSR) as part of public health surveillance were used to determine serological responses to meningococcal vaccines.

To determine persistence of antibody responses to MenC following vaccination with MPSV4 or MenACWY\textsubscript{D}, 1200 subjects, 600 subjects per vaccination group, were randomly selected from DMSS. Basic demographic information, including sex, age and race, and meningococcal vaccination history were obtained from DMSS. Pre-vaccination samples from all subjects were tested to determine baseline levels. Two hundred subjects, 100 subjects per vaccination group, were evaluated during one of six post-vaccination time-points: 5–7 months, 11–13 months, 17–19 months, 23–25 months, 29–31 months, or 35–37 months. Only one post-vaccination sample per subject was tested.

The study was determined exempt from human subjects research review by the Human Subjects Offices at the Naval Health Research Center (NHRC) and Centers for Disease Control and Prevention (CDC).

2.2. Serological responses

Serum bactericidal antibody titers to MenC were measured by a validated rabbit complement serum bactericidal assay (rSBA) using the target strain C11 [12,13]. Viability counts were determined with an automated colony counter (Synbiosis Protocol, United Kingdom). A titer of 1.33 was assigned to sera with no activity in the initial serum dilution of 1:4. Continuous titers were interpolated from 3-fold serum dilutions. Each sample was assigned a continuous
titer resulting in \geq 50\% killing compared to control wells. The proportion of subjects with rSBA titers at or above the putative protective threshold of 8 was calculated [14,15]. A more conservative cutoff of 128 was also used to assess decay of immune responses over time. Serum IgG anticapsular antibody concentrations were determined using a standardized enzyme-linked immunosorbent assay (ELISA) [16]. The concentration of specific IgG antibodies in human sera was calculated relative to a human standard reference serum pool, CDC 1992 [17]. Antibody concentrations below the lower limit of quantitation (LLQ) of 0.001 µg/mL were assigned the LLQ. Data were captured with Gen5™ (BioTek) and analyzed using ELISA for Windows (CDC, Atlanta, GA). The percent of subjects with IgG antibody concentrations at or above 2 µg/mL was determined [18,19]. Testing was performed blinded to vaccine type and time-point.

2.3. Statistical analysis

Sample size calculations with a two-sided alpha of 0.05 and 80% power were based on previous adult immunogenicity studies of meningococcal conjugate and polysaccharide vaccines to determine the proportion of subjects with a threshold of \geq 8 for rSBA titers and \geq 2 µg/mL for IgG responses [8,20]. Statistical analysis was performed using SAS 9.2 (SAS Institute Inc., Cary, NC, USA). Geometric mean titers (GMT) for rSBA and geometric mean concentrations (GMC) for ELISA were calculated for each vaccine group per time-point. Because the log-transformed data were not normally distributed, continuous variables were compared using the Wilcoxon rank sum test at each time point. A Chi-square test was used to compare categorical variables, including the proportions of subjects with rSBA titers \geq 8 and \geq 128, as well as the increase in 4-fold response compared to baseline for each time-point. Comparisons with a two-sided P value \leq 0.05 were considered statistically significant. P-values for multiple tests across the seven time points were adjusted for multiple comparisons by multiplying tested P-values by 7 and comparing them to 0.05 in a test for significance.

3. Results

Among the 1200 subjects evaluated, 83% were male and 68% were white. The mean age at the time of vaccination was 20.5 years (range, 17–37) for MenACWYD and 20.0 years for MPSV4 (range, 17–34). There were no significant differences in sex and race between vaccine groups. Serum bactericidal activity and antibody concentrations to MenC were measured for all subjects prior to vaccination. Post-vaccination rSBA titers and antibody concentrations were analyzed in 1192 and 1190 subjects, respectively. Reasons for exclusion included insufficient volume for testing and failure to pass rSBA acceptance criteria for a reportable titer. The number of serum samples excluded was similar between vaccine groups.

3.1. MenC serologic responses

Baseline rSBA GMT was <8 for both vaccine groups (Fig. 1a). Five to 7 months after vaccination, rSBA GMT increased to 703 and 1557 in MenACWYD and MPSV4 groups, respectively. GMT decreased by \geq 93\% for both groups by 3 years post-vaccination (GMT 43 and 85 for MenACWYD and MPSV4 groups, respectively). There were no significant
differences in GMT between vaccine groups except at 5–7 months post-vaccination (adjusted \( P < 0.05 \)). GMC were <0.20 µg/mL for both vaccine groups prior to vaccination (Fig. 1b). Anti-MenC GMC increased to 1.07 µg/mL in the MenACWY\_D group and 6.00 µg/mL in the MPSV4 group 5–7 months after vaccination. By 3 years post-vaccination, GMC decreased by 38% (0.66 µg/mL) for MenACWY\_D and 51% (2.95 µg/mL) for MPSV4. GMC were significantly different between vaccine groups for all time-points, with the conjugate vaccine resulting in lower IgG antibody concentrations than the polysaccharide vaccine (adjusted \( P < 0.0035 \)).

### 3.2. Proportion of subjects above a given threshold for Men C

The percentages of subjects achieving a serum bactericidal titer of \( \geq 8 \) and \( \geq 128 \) against MenC and a 4-fold rise compared to baseline are shown in Table 1. The proportion of subjects in both vaccine groups with titers \( \geq 8 \) and \( \geq 128 \) at 3 years compared to 5–7 months post-vaccination decreased by 29–38% and 35–43%, respectively. There were no significant differences between vaccine groups in the proportion of subjects with a titer of \( \geq 8 \), \( \geq 128 \), or 4-fold increase from baseline at any time-point. The proportion of subjects with MenC antibody concentrations \( \geq 2.0 \) µg/mL was significantly lower in the MenACWY\_D group at all post-vaccination time-points (Table 2).

### 4. Discussion

This large-scale observational study of antibody persistence to MenC in U.S. military personnel demonstrates waning of immunity within 3 years following vaccination with either MenACWY\_D or MPSV4. No significant differences between the two vaccine groups were observed in the percentage of subjects at or above an rSBA titer of 8, the putative protective level for MenC. Lower antibody concentrations among MenACWY\_D recipients may be explained by the quantity of antigen in each vaccine as MenACWY\_D contains 1/10 the serogroup C antigen of MPSV4. Despite lower antibody concentrations, functional activity (as measured by rSBA) was comparable between vaccine groups, suggesting other immunologic responses elicited by conjugate vaccines likely contribute to overall protection. Conjugate vaccines are T-dependent and therefore induce immunologic memory and more rapid anamnestic responses after repeated doses, with antibody level typically several folds greater than after initial vaccination. This boost response has been demonstrated after a repeat dose of MenACWY\_CRM 5 years after primary vaccination [21]. Additionally, avidity maturation following initial vaccination elicits highly specific antibodies with greater bactericidal activity, and could thus explain the similarity in rSBA response despite significantly different antibody concentrations between vaccine groups.

The importance of maintaining circulating antibodies to prevent MenC disease has been reported in monovalent MenC conjugate vaccine post-licensure studies in the United Kingdom [22,23]. Previously vaccinated subjects that developed MenC disease demonstrated antibody levels and bactericidal activity comparable to unvaccinated patients, despite evidence of immunologic memory [22]. Anamnestic responses can take up to 5 days to develop and thus may not be sufficiently rapid enough to prevent disease [23].
Several U.S. studies have evaluated MenC antibody persistence greater than 1 year following vaccination with quadrivalent conjugate vaccines in adolescents [7,8,21]. These studies were conducted as extension studies within clinical trials, evaluated antibody persistence in <500 subjects per study, and provided duration of antibody response for only one time-point post-vaccination. Serologic responses varied between studies and could be attributed to differences in study population, type of protein conjugate used in the vaccines, and assay methods and reagents (e.g., complement source). Despite these differences, these studies demonstrated waning of immunity to MenC of 60–72%, 35–80%, and 56% at 2, 3 and 5 years after vaccination, respectively. Additionally, one of the studies suggested early evidence of waning at 2 years following vaccination MenACWY_D and MenACWY_CRM, regardless of brand type [7]. Evaluation of immune responses during the first month following vaccination was not conducted in our study; however, we were able to demonstrate an antibody decay of over 93% in anti-MenC serum bactericidal activity and over 38% in antibody concentrations during multiple sampling periods between 6 months and 3 years following vaccination with MenACWY_D.

Preliminary estimates from a quadrivalent meningococcal conjugate vaccine effectiveness (VE) study conducted in over 60% of the US population demonstrates a decrease in VE from 82% (CI = 54%–93%) for adolescents vaccinated <1 year earlier to 59% (CI = 5%–83%) for those vaccinated 3 to <6 years earlier [24]. These data correlate well with our study in which almost half of MenACWY_D recipients did not demonstrate putative protective titers 3 years following a single dose.

This study supports the recent ACIP recommendation for a booster dose of meningococcal conjugate vaccine for adolescents to maintain protection through late adolescence. Decay in antibody responses following a single dose of MenACWY_D should be used to inform policy recommendations regarding repeat vaccination among military personnel at increased risk. As the routine adolescent booster dose is implemented, continued vaccine effectiveness studies, disease surveillance, and antibody persistence studies will be important to evaluate the impact of the booster dose on duration of protection.

Acknowledgments

We thank Doug Avery, for assistance with quality assurance of serum bactericidal assays, and Julianne Nielsen of the Naval Health Research Center who performed confirmatory assays. We are grateful to the Armed Forces Health Surveillance Center and the Department of Defense Serum Repository for providing the specimens and respective data. The views expressed in this work are those of the authors and do not reflect the official policy of the Department of the Navy, Department of Defense, or the US Government. Approved for public releases; distribution is unlimited. This research has been conducted in compliance with all applicable federal regulations governing the protection of human subjects in research. This work was performed with institutional support provided by the Military Vaccine Agency (MILVAX), Military Infectious Diseases Research Program (MIDRP), contract #W911QY-08-D-022.

Abbreviations

| Abbreviation | Description |
|--------------|-------------|
| ACIP | Advisory Committee on Immunization Practices |
| CDC | Centers for Disease Control and Prevention |
| DMSS | Defense Medical Surveillance System |
References

1. Cohn AC, MacNeil JR, Harrison LH, Hatcher C, Theodore J, Schmidt M, et al. Changes in Neisseria meningitidis disease epidemiology in the United States, 1998–2007: implications for prevention of meningococcal disease. Clin Infect Dis. 2010 Jan; 50(2):184–91. [PubMed: 20001736]
2. Erickson L, De Wals P. Complications and sequelae of meningococcal disease in Quebec, Canada, 1990–1994. Clin Infect Dis. 1998 May; 26(5):1159–64. [PubMed: 9597245]
3. Wang JF, Caugant DA, Morelli G, Koumare B, Achtman M. Antigenic and epidemiologic properties of the ET-37 complex of Neisseria meningitidis. J Infect Dis. 1993 Jun; 167(6):1320–9. [PubMed: 8501321]
4. Macneil JR, Thomas JD, Cohn AC. Meningococcal disease: shifting epidemiology and genetic mechanisms that may contribute to serogroup C virulence. Curr Infect Dis Rep. 2011 Aug; 13(4):374–9. [PubMed: 21603878]
5. Artenstein MS, Schneider H, Tingley MD. Meningococcal infections. 1. Prevalence of serogroups causing disease in US Army personnel in 1964–70. Bull World Health Organ. 1971; 45(3):275–8. [PubMed: 5004110]
6. Bilukha OO, Rosenstein N. Preventionand control of meningococcal disease recommendations of the advisory committee on immunization practices (ACIP). MMWR Recomm Rep. 2005 May; 54(RR-7):1–21.
7. Gill CJ, Baxter R, Anemona A, Ciavarro G, Dull P. Persistence of immune responses after a single dose of Novartis meningococcal serogroup A, C, W-135 and Y CRM-197 conjugate vaccine (Menveo(R)) or Menactra(R) among healthy adolescents. Hum Vaccin. 2010 Nov; 6(11):881–7. [PubMed: 21339701]
8. Keyserling H, Papa T, Koranyi K, Ryall R, Bassily E, Bybel MJ, et al. Safety, immunogenicity, and immune memory of a novel meningococcal (groups A, C, Y, and W-135) polysaccharide diphtheria toxoid conjugate vaccine (MCV-4) in healthy adolescents. Arch Pediatr Adolesc Med. 2005 Oct; 159(10):907–13. [PubMed: 16203934]
9. Broderick MP, Faix DJ, Hansen CJ, Blair PJ. Trends in meningococcal disease in the United States military, 1971–2010. Emerg Infect Dis. 2012 Sep; 18(9):1430–7. [PubMed: 22932005]
10. Rubertone MV, Brundage JF. The Defense Medical Surveillance System and the Department of Defense serum repository: glimpses of the future of public health surveillance. Am J Public Health. 2002 Dec; 92(12):1900–4. [PubMed: 12453804]
11. Armed Forces Health Surveillance Center. Fiscal Year 2011 Report. 2011. Available from: http://www.afhsc.mil/viewDocument?file=AFHSC_AnnualReport_WEB.pdf
12. Borrow R, Carlone GM, Serogroup B. C serum bactericidal assays. Methods Mol Med. 2001; 66:289–304. [PubMed: 21336762]
13. Maslanka SE, Gheesling LL, Libutti DE, Donaldson KB, Harakeh HS, Dykes JK, et al. Standardization and a multilaboratory comparison of Neisseria meningitidis serogroup A and C serum bactericidal assays. The Multilaboratory Study Group. Clin Diagn Lab Immunol. 1997 Mar; 4(2):156–67. [PubMed: 9067649]
14. Andrews N, Borrow R, Miller E. Validation of serological correlate of protection for meningococcal C conjugate vaccine by using efficacy estimates from postlicensure surveillance in England. Clin Diagn Lab Immunol. 2003 Sep; 10(5):780–6. [PubMed: 12965904]
15. Trotter C, Borrow R, Andrews N, Miller E. Seroprevalence of meningococcal serogroup C bactericidal antibody in England and Wales in the pre-vaccination era. Vaccine. 2003 Mar; 21(11–12):1094–8. [PubMed: 12559785]
16. Gheesling LL, Carlone GM, Pais LB, Holder PF, Maslanka SE, Plikaytis BD, et al. Multicenter comparison of Neisseria meningitidis serogroup C anti-capsular polysaccharide antibody levels measured by a standardized enzyme-linked immunosorbent assay. J Clin Microbiol. 1994 Jun; 32(6):1475–82. [PubMed: 8077392]
17. Holder PK, Maslanka SE, Pais LB, Dykes J, Plikaytis BD, Carlone GM. Assignment of Neisseria meningitidis serogroup A and C class-specific anticapsular antibody concentrations to the new standard reference serum CDC1992. Clin Diagn Lab Immunol. 1995 Mar; 2(2):132–7. [PubMed: 7697519]
18. Makela PH, Kayhty H, Weckstrom P, Sivonen A, Renkonen OV. Effect of group-A meningococcal vaccine in army recruits in Finland. Lancet. 1975 Nov; 2(7941):883–6. [PubMed: 53370]
19. Peltola H, Makela H, Kayhty H, Jousimies H, Herva E, Hallstrom K, et al. Clinical efficacy of meningococcus group A capsular polysaccharide vaccine in children three months to five years of age. N Engl J Med. 1977 Sep; 297(13):686–91. [PubMed: 408682]
20. Zangwill KM, Stout RW, Carlone GM, Pais L, Harekeh H, Mitchell S, et al. Duration of antibody response after meningococcal polysaccharide vaccination in US Air Force personnel. J Infect Dis. 1994 Apr; 169(4):847–52. [PubMed: 8133100]
21. Jacobson RM, Jackson LA, Reisinger K, Izu A, Odlrin T, Dull PM. Antibody persistence and response to a booster dose of a quadrivalent conjugate vaccine for meningococcal disease in adolescents. Pediatr Infect Dis J. 2012 Oct.
22. Auckland C, Gray S, Borrow R, Andrews N, Goldblatt D, Ramsay M, et al. Clinical and immunologic risk factors for meningococcal C conjugate vaccine failure in the United Kingdom. J Infect Dis. 2006 Dec; 194(12):1745–52. [PubMed: 17109348]
23. Snape MD, Kelly DF, Salt P, Green S, Snowden C, Diggle L, et al. Serogroup C meningococcal glycoconjugate vaccine in adolescents: persistence of bactericidal antibodies and kinetics of the immune response to a booster vaccine more than 3 years after immunization. Clin Infect Dis. 2006 Dec; 43(11):1387–94. [PubMed: 17083009]
24. Cohn AC, MacNeil JR, Clark TA, Ortega-Sanchez IR, Briere EZ, Meissner HC, et al. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2013 Mar; 62(RR-2):1–28.
Fig. 1.
Box plots of (A) serum bactericidal titers measured by rSBA and (B) antibody concentrations measured by ELISA to MenC by months post-vaccination in MenACWY\textsubscript{D} (gray bars) or MPSV4 (white bars) vaccine recipients. The box is defined by the 25th and 75th percentiles of the distribution; the horizontal line within the box represents the median or 50th percentile and the star (asterisk (*)) signifies the mean. Vertical lines extend to the most extreme observation that is less than 1.5× the interquartile distance (75th–25th percentiles) and the diamonds (◇) and boxes (□) correspond to moderate and severe...
outlying assay values, respectively. Cross bars (†) denote statistical significance ($P < 0.05$) between vaccine groups for that time-point.
| Months after vaccination | Number of subjects | Percent with ≥8 | Percent with ≥128 | Percent with ≥4-fold rise compared to baseline |
|-------------------------|-------------------|----------------|------------------|---------------------------------------------|
|                         | MenACWY<sub>D</sub> | MPSV4          | MenACWY<sub>D</sub> | MPSV4                                      |
| Pre                     | 600               | 600            | 21               | 23                                         |
| 5–7                     | 99                | 99             | 87               | 99                                         |
| 11–13                   | 99                | 99             | 87               | 99                                         |
| 17–19                   | 99                | 99             | 87               | 99                                         |
| 23–25                   | 99                | 99             | 87               | 99                                         |
| 29–31                   | 99                | 99             | 87               | 99                                         |
| 35–37                   | 100               | 100            | 62               | 62                                         |
Table 2
Proportion of subjects with antibody concentration $\geq 2$ µg/mL to meningococcal serogroup C by time since vaccination with MenACWY$_D$ or MPSV4.

| Months after vaccination | Number of subjects | Percent with anti-MenC IgG $\geq 2$ µg/mL |
|-------------------------|--------------------|------------------------------------------|
|                         | MenACWY$_D$ | MPSV4 | MenACWY$_D$ | MPSV4 |
| Pre                     | 600          | 600   | 10          | 7     |
| 5–7$^a$                 | 98           | 99    | 39          | 75    |
| 11–13$^a$               | 99           | 99    | 34          | 67    |
| 17–19$^a$               | 99           | 100   | 22          | 70    |
| 23–25$^a$               | 100          | 99    | 23          | 59    |
| 29–31$^a$               | 99           | 98    | 22          | 62    |
| 35–37$^a$               | 100          | 100   | 37          | 67    |

$^a$ P < 0.05, level of significance.