*Clinical Infectious Diseases*

BRIEF REPORT

# Low Meningococcal Vaccination Rates Among Patients With Newly Diagnosed Complement Component Deficiencies in the United States

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Meningococcal vaccination is recommended for patients with complement component deficiencies (CDs) in the United States. In this retrospective database study, only 4.6% and 2.2% of patients received MenACWY and MenB vaccination, respectively, within 3 years of CD diagnosis. Thus, meningococcal vaccination rates among patients with CDs need to be improved.

**Keywords.** meningococcal vaccine; complement component deficiencies; meningococcal serogroups A, C, W, and Y (MenACWY); meningococcal serogroup B (MenB).

Patients with complement component deficiencies (CDs)—particularly those with terminal complement deficiencies—have a greatly increased risk of invasive meningococcal disease [1, 2], which can be associated with severe morbidity and mortality [3]. They are also at increased risk of various other infections [1, 2]. Vaccination of patients with CDs against meningococcal (and pneumococcal) diseases is therefore recommended in the United States [4]. Before 2005, quadrivalent meningococcal (serogroups A, C, W, and Y) polysaccharide vaccine (MPSV4) was recommended for patients with CDs [5]. Meningococcal tetravalent diphtheria toxoid conjugate vaccine (MenACWY-D) was included in the recommendation in 2005 [6], and in 2010, a 2-dose primary series (of MenACWY-D or meningococcal quadrivalent CRM197 conjugate vaccine [MenACWY-CRM]) was recommended for high-risk persons, with a booster dose every 5 years [7]. Meningococcal serogroup B (MenB) vaccine was included in 2015 for those aged 10 years and older [8]. Despite these long-standing recommendations, to our knowledge, there have been no data published on the uptake of meningococcal vaccines in this high-risk population in the United States. The current study determined the uptake and time to receipt of meningococcal vaccines among patients with newly diagnosed CD.

## METHODS

### Study Design

This nationwide retrospective study used data from the de-identified Optum Research Database [9]; hence, informed consent was not required. Uptake and time to receipt of MenACWY and MenB vaccines among patients with newly diagnosed CD were examined.

The study period was January 2005 through September 2018. For the MenACWY analyses, patients were identified during January 2010 through March 2018, as a 2-dose series was first recommended for patients with CD by the Advisory Committee on Immunization Practices (ACIP) in 2010 [7]. For the MenB analyses, patients were identified during January 2015 through March 2018, as the ACIP recommendation to vaccinate those with CD against MenB was made in 2015 [8]. The index date was the first date with an International Classification of Diseases (ICD) diagnosis code for CD (ICD, Ninth Revision [ICD-9], code 279.8; ICD, Tenth Revision [ICD-10], code D841).

### Patients

Inclusion criteria were as follows: 1 or more inpatient or 2 or more outpatient claims (≥30 days apart) with an ICD CD diagnosis code, age 2 years or older (MenACWY) or 10 years or older (MenB) in the index year, and continuous enrollment for 12 months or more before and 6 months or more after the index date (follow-up). Patients were followed for a maximum of 60 months or until disenrollment, whichever came first. In order to capture only newly diagnosed patients, all available continuously enrolled pre-index data (after January 2005) were examined. Baseline characteristics were examined during the 12 months before the index date.

Exclusion criteria were evidence of any condition(s) for which meningococcal vaccination is recommended (asplenia [including sickle cell disease], CD, human immunodeficiency virus [HIV] infection, or eculizumab treatment) during the 12-month-or-more look-back period and evidence of any additional high-risk conditions (asplenia, HIV, eculizumab) on the index date.

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### Outcomes

The co-primary outcomes were uptake and time to receipt of 1 or more dose of a MenACWY vaccine (MenACWY-CRM [GSK], MenACWY-D [Sanofi Pasteur], or MPSV4 [Sanofi Pasteur]) and, separately, a MenB vaccine (meningococcal B 4-component [MenB-4C; GSK] or meningococcal B factor H binding protein [MenB-FHbp; Pfizer]) following a new diagnosis of CD. Outcomes were assessed during the 6- to 60-month follow-up period.

Secondary outcomes were uptake and time to receipt of 2 or more doses of any meningococcal vaccine—separately for MenACWY and MenB—among patients who received a first dose and had 12 months or more of continuous enrollment after the first dose.

### Statistical Analysis

Baseline variables were analyzed descriptively, and data are provided as numbers and percentages for categorical variables and as means and standard deviations (SDs) for continuous variables. The percentages of patients who received 1 or more dose of MenACWY, 1 or more dose of MenB, 2 or more doses of MenACWY, and 2 or more doses of MenB were each estimated using Kaplan–Meier analysis. Total vaccine uptake by age and by provider type (overall and by age group [2–10, 11–18, and ≥19 years]) is also described.

## RESULTS

### Baseline Characteristics

Overall, 1470 MenACWY-eligible patients (mean [SD] age: 40.9 [17.8] years) and 396 MenB-eligible patients (mean [SD] age: 42.9 [16.1] years) were included in the primary analyses (Supplementary Figure 1, Supplementary Table 1). Most patients were aged 19 years or older (84.8% and 88.4%, respectively). Other baseline data are shown in Supplementary Table 1.

### Vaccine Uptake and Time to Receipt

During the 3 years after a CD diagnosis, Kaplan–Meier analysis estimated that only 4.6% of MenACWY-eligible patients received 1 or more dose of a MenACWY vaccine (Figure 1A) and only 2.2% of MenB-eligible patients received 1 or more dose of a MenB vaccine (Figure 1A).

Among those who received a first dose of a MenACWY vaccine and had sufficient follow-up data available (n = 48), only 4.4% were estimated to have received a second dose within 1 year of the first dose, whereas 5 of the 6 who received a first dose of a MenB vaccine were estimated to have received a second dose by 1 year (Figure 1B).

### Vaccination by Age

During all available follow-up, a total of 65 of 1470 (4.4%) MenACWY-eligible individuals received a MenACWY vaccine, but vaccination was much more likely among children and adolescents than adults (12/106 [11.3%] among those 2–10 years of age; 35/118 [29.7%] among those 11–18 years; 14/902 [1.6%] among those 19–55 years; and 4/344 [1.2%] among those ≥56 years). The only recipients of MenB vaccination were children and adolescents (6/46 [13.0%] among those 10–18 years of age; 0/350 [0.0%] among those ≥19 years).

### Vaccination Provider Types

Pediatricians were the most common provider type for MenACWY vaccination, administering 58.5% overall and 91.7% and 68.6% among those aged 2–10 and 11–18 years, respectively (Supplementary Figure 2). Provider types varied widely for adults who received MenACWY vaccination (Supplementary Figure 2). Overall, 58.5% of the MenACWY vaccinations were given at well-care visits. Of the 6 children and adolescents who received MenB vaccination, 4 were given by pediatricians (Supplementary Figure 2).

## DISCUSSION

In this nationwide retrospective database study, only 4.6% and 2.2% of patients were estimated to have received MenACWY and MenB vaccinations, respectively, during the 3 years after a new CD diagnosis. Estimated uptake of a second dose of a MenACWY vaccine was also low (4.4% within 1 year). Although the estimated uptake of a second dose of a MenB vaccine was much higher (83.3% within 1 year), as only 6 patients received a first dose, these results should be interpreted with caution. However, this higher rate could be due to MenB vaccination being labeled and recommended as a multidose series, while MenACWY vaccination can sometimes be given as a single dose [4, 10].

In a previous study, carried out using very similar methodology, uptake of meningococcal vaccines among patients with newly diagnosed asplenia (which carries the same recommendations as CD) was also suboptimal [11]. However, it was notably higher than among patients with CDs in the current study (28.1% for MenACWY and 9.7% for MenB, both at 3 years) [11].

MenACWY vaccination rates in the current study were considerably higher among those aged 11–18 years than among those aged 19 years or older (29.7% vs 1.4%). Given that MenACWY vaccination is routinely recommended at ages 11–12 and 16 years in the United States [10], it seems likely that some of the MenACWY vaccinations in the 11–18-year age group were coincidental routine age-related vaccinations rather than given intentionally for a CD diagnosis. Similarly, MenB vaccination rates were 13.0% among those aged 10–18 years versus 0.0% among those aged 19 years or older; these MenB vaccinations could also have been coincidental, as MenB vaccination is recommended for those aged 16–23 years (preferred for 16–18 years) based on shared clinical decision making [4, 10]. It could also be that pediatricians and other physicians who routinely vaccinate children and adolescents are more aware of the meningococcal vaccination recommendations, including those for at-risk populations.

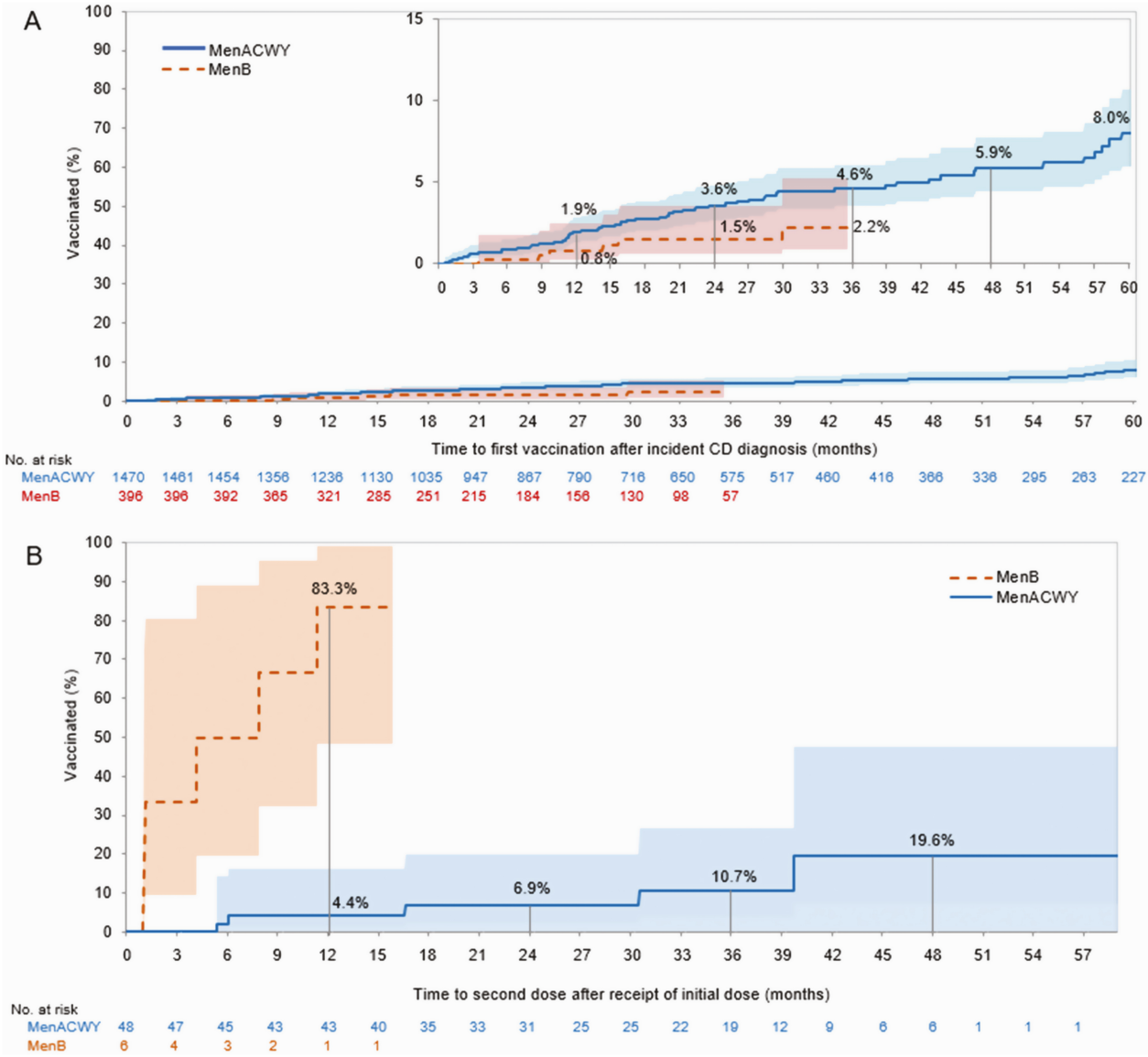


**Figure 1.** Kaplan–Meier cumulative incidence curves of uptake of (*A*) ≥1 dose of a MenACWY vaccine[a] (6–60 months of follow-up) or a MenB vaccine[b] (6–36 months of follow-up) among patients newly diagnosed with CD; (*B*) uptake of a second dose of a MenACWY or MenB vaccine[a,b] among those who received a first dose and had ≥12 months of continuous enrollment after the first dose. Shaded areas show 95% confidence intervals, calculated using the pointwise method. [a]MenACWY vaccines included MenACWY-D, MenACWY-CRM, and MPSV4. [b]MenB vaccines included MenB-4C or MenB-FHbp. Abbreviations: CD, complement component deficiencies; MenACWY, meningococcal serogroups A, C, W, Y; MenACWY-CRM, meningococcal quadrivalent CRM197 conjugate vaccine; MenACWY-D, meningococcal tetravalent diphtheria toxoid conjugate vaccine; MenB, meningococcal serogroup B; MenB-4C, meningococcal B 4-component; MenB-FHbp, meningococcal B factor H binding protein; MPSV4, quadrivalent meningococcal polysaccharide vaccine.

The 2020 ACIP meningococcal vaccination recommendations provide much more detailed recommendations for people with persistent complement deficiencies, including spacing of doses, boosters, etc., by age and vaccine brand [12].

### Strengths and Limitations

Strengths of the current study include the steps taken to only include patients with newly diagnosed CDs, the variable observation period (to maximize sample size and observation time), and the wide US geographic distribution represented in the database. However, the ICD codes used to identify patients with CDs are broad and include CDs that may not confer an increased risk of infection. Some included patients may, therefore, not have been considered at high risk for meningococcal disease. Last, as the data were from managed-care patients with US commercial insurance, these results may not be generalizable to populations who have other types of insurance or who are uninsured.

### Conclusions

Meningococcal vaccination rates among adults with newly diagnosed CDs were extremely low, despite recommendations to vaccinate this at-risk population. Even among those who

received meningococcal vaccination, the time to first vaccination following a new diagnosis of CD was long, as was the time between first and second dose receipt. These results highlight a crucial need to increase the coverage of meningococcal vaccinations among patients with CDs.

## Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

## Notes

***Author contributions.*** L. G. S. B., G. S. M., A. R. B., E. K., P. N., and C. S. H. were involved in the conception or the design of the study. L. G. S. B., A. R. B., E. K., and C. S. H. participated in the collection or generation of the study data. P. K. G., L. G. S. B., G. S. M., A. R. B., T. B., E. K., and C. S. H. were involved in the analyses or interpretation of the data. A. R. B. had full access to all of the data in the study and takes full responsibility for the integrity of the data and the accuracy of the data analysis. All authors participated in the development of this manuscript, had full access to the data, and gave final approval before submission.

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***Potential conflicts of interest.*** P. K. G., P. N. and C. S. H. were employed by the GSK group of companies at the time of the study conduct and/or manuscript development and are shareholders in the GSK group of companies. P. K. G. reports travel support from the GSK group of companies. P. K. G. and P. N. are currently employees of and shareholders in Moderna, Inc. C. S. H. is currently an employee of BMS. L. G. S. B., A. R. B., E. K., and T. B. are employees of Optum, which was contracted by the GSK group of companies to conduct this research. T. B. is a shareholder in UnitedHealth Group. G. S. M. reports involvement as an investigator and consultant for the GSK group of companies, Merck, Seqirus, Pfizer, and Sanofi Pasteur (investigator on clinical trials contracts with University of Louisville), and also as a speaker for Pfizer and Sanofi Pasteur; reports funding for scientific advisory board meetings for the GSK group of companies, Merck, Pfizer, Sanofi Pasteur, and Seqirus. P. K. G. reports travel support from the GSK group of companies. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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