

Brief report

Survey of pediatricians in Germany reveals important challenges for possible implementation of meningococcal B vaccination



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ABSTRACT

Incidence of invasive meningococcal disease is low in Germany at 0.5 cases/100,000 inhabitants. Serogroup B (MenB) is most common, causing 70% of cases, with highest incidence in infants (5.9/100,000). In 2013, a MenB vaccine was licensed in Europe. To assess pediatricians' attitudes towards MenB vaccination and its potential use in Germany we conducted a nationwide cross-sectional survey among 5677 pediatricians. Of 3107 participants (response: 55%), 79.1% would recommend a MenB vaccination to parents, with 66.7% favoring a schedule at 6, 8 and 12 months over 2, 3, 4 and 12 months (13.4%). Administration separately from other vaccines was preferred (63.2%); 38.5% feared that a recommendation would lead to refusal of other recommended vaccinations. In conclusion, pediatricians showed distinct preferences regarding possible integration of MenB vaccination into the existent immunization schedule. As physicians play a crucial role in the implementation, findings will be useful in decision-making regarding potential introduction.

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1. Background

In Germany, the incidence of invasive meningococcal disease (IMD) has shown a decreasing trend since 2003, with a mean annual incidence of 0.5 cases/100,000 inhabitants in 2009–2011. This is lower than the mean incidence in Europe of 0.8 in 2011, and markedly lower than in Ireland (2.0), the UK (1.7) or Spain (1.0) [1]. Approximately 70% of IMD was caused by meningococcal serogroup B (MenB), with a case-fatality of 8.2% [2]. MenB IMD incidence was highest in infants (mean: 5.9/100,000; 16% of all cases), followed by 1, 2 and 15–19 year olds (3.3, 1.7 and 1.1/100,000, respectively). Of cases in infants, 48% occurred in the first 6 months of life. Longterm sequelae such as hearing loss, neurological defects or amputations have been reported in up to ~20% of cases [3,4].

In January 2013, the European Medicines Agency licensed 4CMenB (Bexsero®), a novel multi-component MenB vaccine based on subcapsular proteins [5]. Strain coverage for Germany was estimated at 82% [6]. In pre-licensure studies, the vaccine induced satisfactory immunogenicity; but definitive data on effect on

meningococcal carriage, vaccine effectiveness and rare adverse events are still pending [7]. The number of required doses varies from 2 to 3 primary immunizations with/without 1 booster, depending on age at first dose [8]. Reactogenicity of Bexsero® is increased particularly in infants when administered concomitantly with routine vaccines (Infanrix hexa® and Prevenar®) compared to routine vaccines only or Bexsero® only [9].

Bexsero® was marketed in Germany in December 2013. To be included in the German national immunization schedule and reimbursed by statutory health insurance, a new vaccine must be recommended by the German Standing Committee on Vaccination (STIKO). STIKO recommendations are officially endorsed by 15 of the 16 federal states. While not legally binding, these recommendations are considered the medical standard in liability cases [10]. The currently recommended infant immunization schedule is shown in Fig. 1. Childhood immunizations are almost exclusively administered by privately practicing pediatricians on a fee-for-service basis [11]. In developing evidence-based recommendations, STIKO follows a standard operating procedure to evaluate all available evidence on vaccine efficacy/effectiveness and safety, but also on other aspects, such as implementability of the potential recommendation, including possible obstacles and likely acceptance of the vaccine [12]. Physicians play a crucial role for acceptance: in a representative survey among parents in Germany, 93% indicated that the physician was the main source of information regarding

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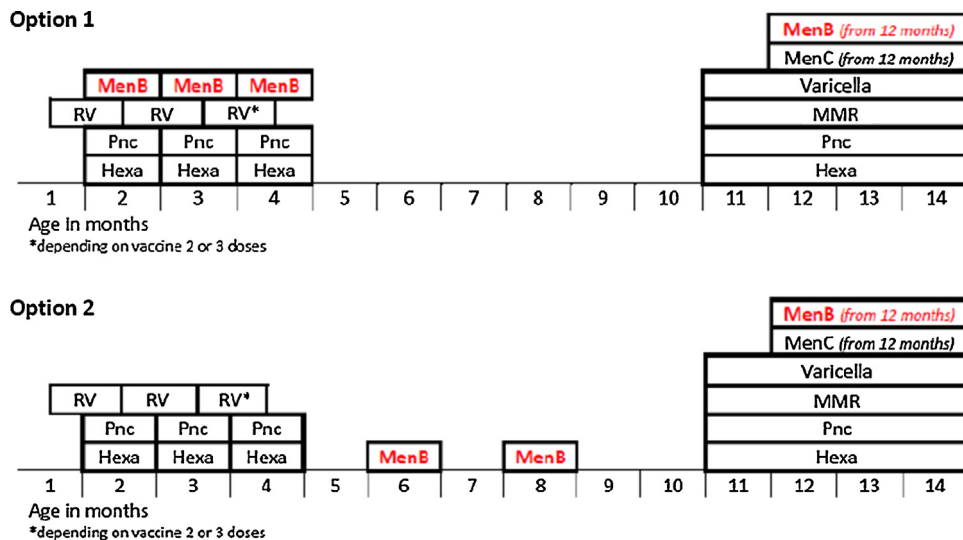


Fig. 1. Current routine vaccination schedule for infants 0–14 months as recommended by the German Standing Committee on Vaccination (STIKO), including the potential, currently not recommended meningococcal B vaccinations (in red) at months 2, 3, 4 and 12 (Option 1) and at months 6, 8 and 12 (Option 2). Abbreviations: Hexa—hexavalent vaccination (diphtheria, tetanus, polio, pertussis, Haemophilus influenzae type b and hepatitis B), MMR—measles mumps rubella vaccination, MenB—meningococcal B vaccination, MenC—meningococcal C vaccination, Pnc—pneumococcal vaccination, RV—rotavirus vaccination.

vaccination [13]. Another German study found that physicians' attitudes toward vaccination are predictive of vaccination coverage [14]. Similarly, a survey in Australia described that parents' potential willingness to have their child receive Bexsero® was most strongly influenced by a recommendation of the family doctor [15].

The aim of our study was to assess attitudes among pediatricians towards MenB vaccination and its potential use in Germany, with an emphasis on the perceived need for such a vaccine, the feasibility of integrating it into the existing immunization schedule and possible implications for other routine childhood vaccinations.

2. Material and methods

In November 2013, we conducted a nationwide cross-sectional survey among the 5677 privately practicing pediatricians with membership in the German Professional Association for Pediatricians (BVKJ), representing 96% of all privately practicing pediatricians in Germany [16].

A written questionnaire was developed that included items on participants' demographics (age, sex, practice location, years spent in pediatric practice and board certification status), as well as on their views regarding a possible MenB vaccine recommendation and administration (Table 1). The questionnaire was pre-tested by 15 pediatricians and subsequently posted to all eligible members, accompanied by a cover letter and one-page background information on Bexsero® and MenB IMD epidemiology in Germany.

Returned questionnaires were double-entered electronically using EpiData version 3.1 (EpiData Association, Denmark). A descriptive analysis was performed, including calculation of proportions and 95% confidence intervals (CI). Demographic data on participants were compared to available BVKJ-member information. Due to Germany's geographical size and historical differences, we performed regional analyses. We explored associations using the Chi-squared Test and univariate logistic regression, followed by stratification for duration in private practice, sex and region to estimate odds ratios (ORs) with 95% CIs. Statistical analysis was performed using Stata® version 13 (StataCorp, Texas, USA).

3. Results and discussion

Of the 5677 questionnaires sent out, 3107 (55%) were returned. Respondents' mean age was 53 years (all BVKJ-members: 54 years),

52% were male (all members: 50%), and response ranged from 53–58% per region. Mean duration in pediatric practice was 16 years, and 99% ($n = 3070$) were board-certified pediatricians.

Participants' responses are summarized in Table 1. The majority (79.1%) stated they would recommend MenB vaccination. The most common reasons given for not recommending the vaccine were a concern that the schedule would become overcrowded and insufficient data on potential rare adverse events. Children ≤ 24 months were most frequently specified as target groups for MenB vaccination, in keeping with the highest incidence at these ages. Two thirds of participants believed that parents would be acceptant of an official STIKO recommendation.

Of two possible licensed vaccine schedules integrating MenB vaccination into the current German routine immunization schedule, vaccination at month 6, 8 and 12 of age (Option 2, Fig. 1) was preferred by 66.7% of physicians (95%CI 65.0–68.3; $n = 2070$), whereas vaccination at month 2, 3, 4 and 12 (Option 1, Fig. 1) was favored by only 13.4% (95%CI 12.2–14.6; $n = 416$). Neither schedule was chosen by 14% (95%CI 13.0–15.5; $n = 441$). Of these, 59.6% (95%CI 54.9–64.3%; $n = 263$) indicated they would vaccinate in the first 6 months of life but at different time points than in Option 1. In keeping with the strong preference for Option 2, only 31.3% of all respondents thought MenB vaccination should be administered concomitantly with other standard vaccinations. Similarly, >70% of all participants objected in principle to the simultaneous administration of 3 vaccines; 19.7% among those favoring Option 1 and 81.8% among those favoring Option 2 ($p < 0.005$). The most common reason given for objection was lack of parental acceptance (Table 1).

Approximately 40% of all respondents thought that recommendation of MenB vaccine would lead to refusal of other recommended vaccinations (Table 1). It seems surprising that physicians thought parents would most likely forego pneumococcal vaccination if MenB vaccination were introduced, since this is a disease at least as severe as MenB IMD with a higher pre-vaccination incidence [17], but maybe less in the focus of privately practicing than of hospital-based pediatricians [18]. However, the other three vaccines named in this context either protect against diseases that are perceived as less severe (rotavirus, varicella) or with a lower risk of infection than MenB IMD (MenC).

Age, sex, region and years spent in pediatric practice had a significant effect on some of the responses (Table 2). As age of pediatrician and years in practice were highly correlated

Table 1Survey results among privately practicing pediatricians ($n = 3107$), November 2013, Germany.

Item	<i>n</i>	%	95% CI ^c
If a MenB ^a vaccine were available: Would you recommend the vaccination to parents for their child (irrespective of an inclusion in the national immunization schedule)?			
Yes	2456	79.1	77.6–80.5
For what age groups? ^b			
<12 months	1874	76.3	74.6–78.0
12–23 months	1389	56.6	54.6–58.5
2–11 years	850	34.6	32.7–36.5
12–17 years	918	37.4	35.5–39.3
≥18 years	269	11.0	9.7–12.3
No	345	11.1	10.0–12.3
Why not? ^b			
Would make vaccination schedule too crowded	187	54.1	48.6–59.4
Data on rare adverse events insufficient	163	47.1	41.8–52.5
Disease is too rare	81	23.4	19.0–28.2
Vaccination causes too many adverse events	55	15.9	12.2–20.2
Don't know	259	8.3	7.4–9.4
Do you believe that parents will be acceptant of an official recommendation for routine MenB ^a vaccination of infants?			
Yes	2077	66.9	65.2–68.5
No	371	11.9	10.8–13.1
Don't know	620	20.0	18.6–21.4
If MenB ^a vaccination is adopted in the routine immunization schedule:How should infants be vaccinated against meningococcal B?			
Separately from other recommended standard vaccinations	1963	63.2	61.5–64.9
Both options (concomitant and separately) are acceptable	761	24.5	23.0–26.0
Concomitantly with hexavalent and pneumococcal vaccination	210	6.8	5.9–7.7
Don't know	111	3.6	2.9–4.3
Would you conceivably administer three vaccines simultaneously to infants and toddlers at one visit?			
Yes	662	21.3	19.9–22.8
No	2293	73.8	72.2–75.3
Why? ^b			
Lack of parents' acceptance	2053	89.5	88.2–90.6
Too hard on the child	1611	70.3	68.3–72.1
Potential adverse events cannot be attributed clearly to one/the new vaccine	1384	60.4	58.3–62.4
Causes increased reactogenicity that I would not want to risk	1313	57.3	55.2–59.3
Not compatible with practice logistics	146	6.4	5.4–7.4
Don't know	133	4.3	3.6–5.1
Do you fear that integration of the MenB ^a vaccine into the routine vaccination schedule for infants <1 year would lead to a refusal of other recommended vaccines?			
Yes	1195	38.5	36.7–40.2
Which ones? ^b			
Pneumococcal vaccine	568	47.5	44.6–50.4
Rotavirus	455	38.0	35.3–40.9
Meningococcal C	431	36.0	33.3–38.8
Varicella	418	35.0	32.2–37.7
Hexavalent vaccine	53	4.4	3.3–5.8
Measles–Mumps–Rubella	31	2.6	1.8–3.7
Don't know	196	16.4	14.3–18.6
No	1612	51.9	50.1–53.7
Don't know	269	8.7	7.7–9.7

^a MenB: meningococcal serogroup B.^b Multiple answers possible.^c CI: confidence interval.

(Pearson's correlation coefficient = 0.83, $p < 0.005$), we present results only for the latter. Female physicians and physicians in practice ≥ 10 years were less likely to fear refusal of other recommended vaccines if MenB vaccination were introduced, but were more likely to object to simultaneous administration of three vaccines or concomitant MenB vaccination and other vaccines. Correspondingly, female physicians were less likely to prefer Option 1 than their male colleagues, especially females in practice > 10 years (see Appendix).

Compared to pediatricians from Northern states, pediatricians from Western and Eastern states were more likely and pediatricians from Southern states less likely to believe that parents would be acceptant of MenB vaccination. Southern pediatricians were also more likely to fear refusal of other vaccines if MenB vaccination were recommended, particularly if in practice < 10 years, while those in Eastern states were less likely to fear this, particularly those in practice ≥ 20 years (Appendix). This corresponds with a lower uptake of standard vaccines in Southern states than

in other parts of Germany [19], possibly explained by a higher percentage of anthroposophists/vaccine-sceptics in their population [20,21] and a less positive physicians' attitude towards vaccination [14]. In contrast, uptake of standard vaccines is highest in Eastern Germany [19], where pediatricians, particularly female pediatricians (Appendix), were most likely to recommend MenB vaccination. Nonetheless, Eastern pediatricians were also more likely to object to simultaneous administration of 3 vaccines and prefer Option 2. Regional differences among German physicians were also seen in a previous study regarding attitude towards pertussis and measles vaccination [14].

As physicians play a crucial role in the implementation and acceptance of new vaccines, assessment of their views is essential. So far, results from only one other study, conducted in 2012 in France, are available on the attitude of pediatricians and general practitioners towards MenB vaccination [22]. In this study, 96% of responding physicians thought MenB vaccination important, but 81% were against administering three vaccines

Table 2
Influence of length of time in practice, sex and region of private practice on pediatricians' responses. Only variables with statistically significant associations in univariate analysis are shown.

Item	N	%	OR	95% CI ^c
Would recommend MenB ^a vaccination to parents				
Region ^b				
North	369	86.0	Ref	–
West	810	88.2	1.22	0.87–1.71
East	485	92.4	1.97	1.29–3.01
South	744	85.4	0.95	0.68–1.33
In favor of administering MenB ^a vaccination concomitantly with the hexavalent and pneumococcal vaccine				
Length of practice time				
<10 years	276	36.8	Ref	–
10–19 years	343	33.8	0.88	0.72–1.07
≥20 years	349	30.5	0.75	0.62–0.92
Sex of pediatrician				
Female	404	29.0	Ref	–
Male	565	37.0	1.44	1.23–1.68
Would conceivably administer 3 injections to infants and toddlers at one visit				
Length of practice time				
<10 years	215	28.9	Ref	–
10–19 years	220	21.6	0.68	0.54–0.84
≥20 years	225	19.2	0.58	0.47–0.72
Sex of pediatrician				
Female	222	15.9	Ref	–
Male	438	28.1	2.06	1.72–2.47
Region ^b				
North	120	26.6	Ref	–
West	235	24.2	0.88	0.69–1.14
East	75	13.8	0.44	0.32–0.61
South	652	22.5	0.86	0.67–1.12
Preference for schedule Option 1 (MenB ^a vaccine doses at 2, 3, 4 and 12 months)				
Sex of pediatrician				
Female	155	13.5	Ref	–
Male	260	19.6	1.56	1.26–1.94
Region ^b				
North	78	20.6	Ref	–
West	138	16.8	0.78	0.57–1.06
East	54	12.3	0.54	0.37–0.79
South	142	17.8	0.84	0.61–1.14
Belief that parents will be acceptant of routine infant MenB ^a vaccination				
Sex of pediatrician				
Female	992	86.9	Ref	–
Male	1078	83.2	0.75	0.60–0.94
Region ^b				
North	310	82.2	Ref	–
West	732	89.6	1.86	1.32–2.63
East	431	92.1	2.52	1.64–3.86
South	567	76.9	0.72	0.53–0.99
Fear that MenB ^a vaccination will lead to refusal of other recommended vaccines				
Length of practice time				
<10 years	348	49.7	Ref	–
10–19 years	441	44.6	0.82	0.67–0.99
≥20 years	388	35.6	0.56	0.46–0.68
Sex of pediatrician				
Female	512	39.0	Ref	–
Male	675	45.5	1.31	1.12–1.52
Region ^b				
North	188	43.6	Ref	–
West	366	39.6	0.85	0.67–1.07
East	173	34.0	0.67	0.51–0.87
South	441	49.6	1.27	1.01–1.60

^a MenB: meningococcal serogroup B.

^b Regions were defined as following: North (federal states of Bremen, Hamburg, Lower Saxony, Schleswig-Holstein), West (Hesse, North Rhine-Westphalia, Rhineland-Palatinate, Saarland), East (Berlin, Brandenburg, Mecklenburg-Western Pomerania, Saxony, Saxony-Anhalt, Thuringia) and South (Baden-Württemberg, Bavaria).

^c CI: confidence interval.

simultaneously and 54% favored administering MenB vaccine separately from other vaccinations—results comparable to ours. Thus, the addition of Bexsero[®] to an already busy vaccination schedule appears challenging, at least in the first 6 months of life, primarily due to widespread reluctance to administer three injections simultaneously and thus to administer Bexsero[®] concomitantly with currently recommended standard vaccines. Moreover, 90%

of pediatricians who objected to three simultaneous injections believed that parents would also object to this. A recent review of mostly North American studies on provider and parental attitudes towards multiple injections [23] showed that provider acceptance of >2 injections increased when official recommendations required this. Providers also tended to overestimate parental concern, and reassurance by physicians as well as an understanding of the

severity of the target disease increased parental acceptance of multiple injections. While parental objection to >2 injections per visit was also reported in a recent study from The Netherlands [24], with a majority of parents preferring an extra visit, half said they would probably accept three vaccinations if actually offered. Similarly, the Australian survey showed that a third injection per visit made only 15% of parents less likely to want MenB vaccine for their child [15]. However, none of the studies, including the latter, explicitly investigated whether parental acceptance for concomitant vaccination would be affected by the information that concomitant vaccination was shown to be more reactogenic than alternating injections.

Taken together, our results suggest that if STIKO should recommend MenB vaccination for infants from 2 months of age on completion of the evidence assessment, it would be essential to provide pediatricians with a convincing rationale and strong arguments for concomitant vaccination, to ensure successful implementation and to avoid the dropping of other equally or even more important vaccinations by physicians or parents. This should include evidence suggesting that parents can be convinced to accept three simultaneous injections by their physicians. Since MenB incidence is highest in the first year of life, with about half of cases occurring <6 months of age, early vaccination would prevent the most cases. Nonetheless, in Germany 59% of cases in the first 3 years of life occur in children aged 9 months and older, the age-span in which protection would be expected using the later 3-dose schedule. An additional 21% of cases in children <3 years of age occur in children from 5 to 8 months of age (unpublished data,

Robert Koch Institute), potentially preventable through earlier vaccination. Thus, in view of the currently low incidence in Germany and overwhelming preference for administration of MenB vaccine separately from routine vaccines, implementation at a later age, requiring fewer doses, might lead to higher uptake and thereby have similar or higher impact. A modeling exercise comparing the impact of different vaccination strategies at the population level is currently being carried out for Germany and will inform STIKO decision-making in addition to other data such as the results derived from the present survey.

Acknowledgments

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Conflict of interest

None of the authors report potential conflicts of interest.

Appendix A. Appendix:

Table A1.

Table A1

Influence of length of time in practice, sex and region of private practice on pediatricians' responses in univariate and stratified analysis. Results of the stratified analysis are presented only when odds ratios in strata differed markedly from those of the univariate analysis.

Item	N	%	OR	95% CI ^c
Would recommend MenB ^a vaccination to parents				
Length of practice time				
<10 years	617	88.5	Ref	–
10–19 years	870	89.3	1.08	0.80–1.48
≥20 years	948	86.0	0.79	0.59–1.06
Sex of pediatrician				
Female	1141	87.5	Ref	–
Male	1306	88.0	1.04	0.83–1.31
Region ^b				
North	369	86.0	Ref	–
West	810	88.2	1.22	0.87–1.71
East	485	92.4	1.97	1.29–3.01
South	744	85.4	0.95	0.68–1.33
Region ^b by sex: males				
North	204	88.3	Ref	–
West	507	90.2	1.22	0.75–1.99
East	108	90.0	1.19	0.58–2.44
South	465	85.2	0.76	0.48–1.21
Region ^b by sex: females				
North	163	83.2	Ref	–
West	301	85.3	1.17	0.73–1.89
East	377	93.1	2.73	1.59–4.66
South	279	85.9	1.23	0.75–2.00
In favor of administering MenB ^a vaccination concomitantly with the hexavalent and pneumococcal vaccine				
Length of practice time				
<10 years	276	36.8	Ref	–
10–19 years	343	33.8	0.88	0.72–1.07
≥20 years	349	30.5	0.75	0.62–0.92
Sex of pediatrician				
Female	404	29.0	Ref	–
Male	565	37.0	1.44	1.23–1.68
Region ^b				
North	163	35.8	Ref	–
West	336	35.0	0.97	0.77–1.22
East	162	29.9	0.77	0.59–1.00
South	296	32.2	0.85	0.67–1.08

Table A1 (Continued)

Item	N	%	OR	95% CI ^c
<i>Would conceivably administer 3 injections to infants and toddlers at one visit</i>				
Length of practice time				
<10 years	215	28.9	Ref	–
10–19 years	220	21.6	0.68	0.54–0.84
≥20 years	225	19.2	0.58	0.47–0.72
Sex of pediatrician				
Female	222	15.9	Ref	–
Male	438	28.1	2.06	1.72–2.47
Region ^b				
North	120	26.6	Ref	–
West	235	24.2	0.88	0.69–1.14
East	75	13.8	0.44	0.32–0.61
South	652	22.5	0.86	0.67–1.12
<i>Preference for schedule Option 1 (MenB^a vaccine doses at 2, 3, 4 and 12 months)</i>				
Length of practice time				
<10 years	121	18.0	Ref	–
10–19 years	134	15.8	0.86	0.65–1.12
≥20 years	160	16.9	0.92	0.71–1.20
Sex of pediatrician				
Female	155	13.5	Ref	–
Male	260	19.6	1.56	1.26–1.94
Region ^b				
North	78	20.6	Ref	–
West	138	16.8	0.78	0.57–1.06
East	54	12.3	0.54	0.37–0.79
South	142	17.8	0.84	0.61–1.14
<i>Length of practice time by sex: males</i>				
<10 years	59	17.9	Ref	–
10–19 years	39	10.5	1.13	0.79–1.61
≥20 years	56	12.6	1.17	0.82–1.65
<i>Length of practice time by sex: females</i>				
<10 years	62	18.1	Ref	–
10–19 years	95	20.0	0.54	0.35–0.83
≥20 years	103	20.5	0.66	0.44–0.98
<i>Belief that parents will be acceptant of routine infant MenB^a vaccination</i>				
Length of practice time				
<10 years	518	85.2	Ref	–
10–19 years	719	84.0	0.91	0.68–1.22
≥20 years	827	85.8	1.05	0.79–1.40
Sex of pediatrician				
Female	992	86.9	Ref	–
Male	1078	83.2	0.75	0.60–0.94
Region ^b				
North	310	82.2	Ref	–
West	732	89.6	1.86	1.32–2.63
East	431	92.1	2.52	1.64–3.86
South	567	76.9	0.72	0.53–0.99
<i>Fear that MenB^a vaccination will lead to refusal of other recommended vaccines</i>				
Length of practice time				
<10 years	348	49.7	Ref	–
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Region ^b				
North	188	43.6	Ref	–
West	366	39.6	0.85	0.67–1.07
East	173	34.0	0.67	0.51–0.87
South	441	49.6	1.27	1.01–1.60
<i>Region^b by length of practice time: <10 years</i>				
North	55	44.4	Ref	–
West	98	44.3	1.00	0.64–1.56
East	52	44.8	1.02	0.61–1.70
South	135	60.0	1.88	1.21–2.93
<i>Region^b by length of practice time: ≥20 years</i>				
North	63	41.7	Ref	–
West	118	33.8	0.71	0.48–1.06
East	69	26.5	0.50	0.33–0.77
South	132	42.2	1.02	0.69–1.51

^a MenB: meningococcal serogroup B.^b Regions were defined as following: North (federal states of Bremen, Hamburg, Lower Saxony, Schleswig-Holstein), West (Hesse, North Rhine-Westphalia, Rhineland-Palatinate, Saarland), East (Berlin, Brandenburg, Mecklenburg-Western Pomerania, Saxony, Saxony-Anhalt, Thuringia) and South (Baden-Württemberg, Bavaria).^c CI: confidence interval.

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