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Pediatricians' Preferences for Infant Meningococcal Vaccination

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ABSTRACT

Background: Meningococcal disease is rare but can cause death or disabilities. Although the Advisory Committee on Immunization Practices has recommended meningococcal vaccination for at-risk children aged 9 through 23 months, it has not endorsed universal vaccination. Health insurance payments for the vaccination of children who are not at risk are likely to be limited. Use of infant meningococcal vaccines by these families will thus depend on the preferences of physicians who might recommend vaccination to parents, as well as parents' preferences. **Objective:** To quantify pediatricians' preferences for specific features of hypothetical infant meningococcal vaccines. **Methods:** A sample of pediatricians (n = 216) completed a Web-enabled, discrete choice experiment survey in which respondents chose between pairs of hypothetical vaccines in a series of trade-off questions. The questions described vaccines with six attributes. A random-parameters logit regression model was used to estimate the relative importance weights physicians place on vaccine features. These weights were used to calculate the predicted probability that a physician chooses hypothetical vaccines with given characteristics. **Results:** Pediatricians' choices indicated that increases in vaccine effectiveness were among the most important factors in their vaccine recommendations, followed by increases in the number of injections. The age at which protection begins and the number of additional office visits were less important. Whether a booster was required after 5 years was the least important factor in vaccine recommendations. The results suggest that virtually all (99.9%) physicians in the sample would recommend a vaccine even with the least-preferred features rather than no infant meningococcal vaccine. **Conclusions:** Physicians' responses indicate a strong preference for infant meningococcal vaccination.

Keywords: conjoint analysis, discrete choice experiment, infant vaccine, meningococcal disease, preference.

Introduction

Meningococcal disease is a rare infectious disease in the United States, with 845 cases across all ages reported to the National Notifiable Disease Surveillance System in 2010 [1,2]. Incidence is highest among infants younger than 1 year (5.38 cases per 100,000) followed by adolescents (1.73 cases per 100,000) [1,3], while the case-fatality rate is higher among adolescents (10%–14%) than among infants (6%). Furthermore, 11% to 19% of the survivors have permanent sequelae, such as hearing loss, neurologic damage, or loss of a limb [1,4]. Because of the rapid progression of the disease and its severe outcomes, meningococcal disease can cause considerable anxiety among parents and health care providers, and both sporadic cases and outbreaks can place a significant burden on health services (see, e.g., Krause et al. [5] and Osterholm [6]).

The Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination of 11- or 12-year-old children with a quadrivalent meningococcal vaccine (serogroups A, C, Y, and W-135) and a booster at 16 years. In recent years, the US Food and Drug Administration (FDA) licensed two meningococcal vaccines for use in infants, including a two-dose quadrivalent meningococcal vaccine (serogroups A, C, Y, and W-135) for administration beginning as early as age 9 months and a four-dose bivalent combination vaccine (serogroups C and Y and *Haemophilus influenzae* type b) for administration beginning as early as age 6 weeks. As of October 2012, the ACIP recommended that infants with certain risk factors for meningococcal disease receive one of the licensed vaccines but did not endorse universal infant vaccination [4,7]. The primary rationale for this decision was based on the current epidemiology of meningococcal disease. Disease rates have declined in all age groups since 2000 and

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are at historically low levels, and more than one-half of the cases in infants younger than 1 year are caused by serogroup B, which is not prevented by any meningococcal vaccine licensed in the United States [3,4]. In addition, published cost-effectiveness analyses in the United States suggest that meningococcal vaccination is not cost-effective [8–10].

Without a recommendation for universal vaccination, it is unlikely that infant meningococcal vaccination will be covered by the Vaccines for Children program or private health insurance programs for children who are not at risk, though it will be available to families who choose to use it (as well as to those with children who are considered at risk). Thus, the use of infant meningococcal vaccines will depend on physicians' recommendations to parents and parents' willingness to vaccinate their children. There is no quantitative evidence on parent or provider preferences for meningococcal vaccines and vaccination strategies in the United States.

This study aimed to quantify pediatricians' preferences for hypothetical meningococcal vaccines and vaccine features, where ranges of vaccine features were selected to encompass the features of currently available vaccines. The results will indicate the importance that physicians place on infant meningococcal vaccination. The study does not seek to rebut the results of cost-effectiveness analysis. Rather, in contrast to the expert opinion that informs vaccination licensure and recommendation decisions by the FDA and the ACIP, provided by a limited number of empaneled experts, this study quantifies expert opinion using a larger sample of physicians. This is the first study of physician preferences for meningococcal vaccines administered to this age group and only the second study of preferences for meningococcal vaccines in general. Bishai et al. [11] elicited parents' preferences and willingness to pay for meningococcal vaccines for adolescents. Similar methods have been used to quantify preferences for human papilloma virus vaccines in the United States [12] and Vietnam [13] and for vaccines against cholera and typhoid fever [14].

Methods

Study Design

The methodological approach used was a discrete choice experiment (DCE), or choice-format conjoint analysis, which is a valid and reliable survey technique for eliciting trade-offs to quantify the relative importance respondents assign to outcomes and other features of health interventions [15–20]. DCE is based on the premise that the attractiveness of an intervention is a function of its attributes. In particular, the perceived value of an intervention is a weighted sum of the attributes of the intervention, where the weights reflect the sample's average perceived relative importance of each attribute. DCE questions elicit preferences between pairs of hypothetical alternatives, and statistical analysis of the pattern of these choices reveals the relative importance weights respondents place on attributes.

The study followed best-practice guidelines as outlined in the International Society for Pharmacoeconomics and Outcomes Research checklist for conjoint-analysis applications in health [16]. Vaccine attributes were selected to describe hypothetical vaccines in the survey. The selection of attributes was informed by the fact that current and possible future meningococcal vaccines and vaccine strategies can vary in terms of the number of cases prevented, the total number of injections children receive, the additional number of visits to the physicians' offices for vaccination, and the total out-of-pocket costs of vaccines. In addition, the research team, which included clinical experts who reviewed study materials, conducted an informal review of selected published and unpublished health economics, epidemiology, and marketing studies related to infant meningococcal vaccines. A list of possible vaccine attributes was discussed and refined by the study team. Attributes that remained on the list were 1) relevant for defining the clinical features of currently available and potential vaccines; 2) reflected other, nonclinical features of concern to physicians; and 3) incorporated physicians' assessment of patient concerns. If the sources or discussions concluded that an attribute did not meet these criteria or would not distinguish among hypothetical meningococcal vaccines, it was not included in the attribute list. The hypothetical vaccine attributes were evaluated in face-to-face semi-structured interviews with 10 pediatricians in the United States.

The final hypothetical vaccine attributes (Table 1) included vaccine effectiveness (defined in terms of the number of cases of disease, disability, and death prevented over 5 years), age at which protection begins, the number of injections added to the immunization schedule, the number of additional doctors' office visits required to administer the vaccine, whether a booster

Table 1 – Attributes and attribute levels used in conjoint-analysis survey of physicians' preference for infant meningococcal disease vaccination.

Vaccine attribute	Level	
Age at which protection begins	4 mo	
	12 mo	
	2 y	
Number of cases of disease, disability, and death prevented over 5 y	500 cases of disease, 125 cases of disability, and 50 deaths prevented	
	425 cases of disease, 110 cases of disability, and 43 deaths prevented	
	350 cases of disease, 88 cases of disability, and 35 deaths prevented	
	250 cases of disease, 63 cases of disability, and 25 deaths prevented	
Number of injections added to the schedule	0*	
	2	
	4	
Number of additional doctor visits required	0	
	1	
	3	
Booster vaccine needed after 5 y	Yes	
	No	
Total out-of-pocket costs to parents ($)	Narrower cost range	Wider cost range
	0	0
	10	25
	25	75
	75	150

* This represents a meningococcal vaccine administered as a combination vaccine. Because a new combination vaccine may replace one or more existing vaccines or vaccine series, it would be possible for a new vaccine to both have no effect on the number of injections in a particular child's immunization schedule and to require more doctor's visits.

vaccine would be required after 5 years, and total out-of-pocket cost of vaccination for parents. The range of attribute levels was selected using the following criteria: 1) it should span the clinically relevant range of outcomes that has been observed or is likely to be observed with currently available and candidate vaccines; 2) it should span the changes in features likely to be observed in practice; and 3) it should encompass the maximum range over which respondents are willing to accept trade-offs among attributes.

Many of the pediatricians interviewed noted that the cost to parents is an important determinant of whether parents choose to vaccinate and whether they choose to complete a vaccine series. Physicians' proxy assessments of the relative importance of cost to parents, however, cannot be used to calculate welfare-theoretic willingness to pay because physicians' stated vaccine recommendations are not subject to a binding budget constraint. Nevertheless, physicians' perceptions of the importance of costs could be useful in evaluating vaccine policies. Because the costs of many vaccines in the United States either are fully covered by health insurance or are free, we evaluated physicians' attentiveness to the hypothetical costs with a scope test of the internal validity of respondents' sensitivity to absolute differences in costs [21]. The scope test consisted of randomly assigning approximately one-half of respondents to a narrower range of costs ($0–$75) and the other half to a wider range of costs ($0–$150).

Although vaccine safety is important to parents making vaccine choices for their children [22], it was not included among the attributes in the study. Rather, physician respondents were told to assume that all the hypothetical vaccines described in the survey had the same risk of mild side effects, such as injection-site reactions. Respondents were also told that the hypothetical vaccines described in the survey may be different than vaccines that are currently available or in development.

Communicating both the baseline risks of meningococcal disease and changes in that risk due to vaccination is challenging because people often have difficulty evaluating such small incidence rates. Among the errors people make when evaluating risks are disregarding very small probabilities [23], misunderstanding numerical measures of risk by paying more attention to fraction numerators than denominators [24], or subjectively editing small probabilities upward when outcomes are perceived to be severe [25].

To facilitate the communication of meningococcal disease risks and risk changes, risks were presented as frequencies, which are easier to understand than are other statistical formats [26]. The study also incorporated a risk-communication experiment to evaluate whether denominator neglect [24]—a possible bias in risk perception—influenced physicians' preferences for vaccine features. It is believed that respondents rely relatively more on numerators when comparing different risks, leading to misperceptions of risk. To test whether physician respondents were susceptible to this bias, they were randomly assigned to one of two formats for presenting information on the risk of meningococcal disease (Table 2). The first description expressed risks in terms of the number of cases in a constant-base population (constant-base population information format). The second description expressed risks in terms of the size of the base population in which one case would be realized (variable-base population information format).

To create hypothetical vaccine profiles for the recommendation questions, we used an SAS implementation of a commonly used algorithm to generate an unlabeled, D-efficient, fractional factorial experimental design that resulted in 36 hypothetical vaccine pairs [27–30]. Because the quality of responses to choice questions declines when the number of choice questions leads to fatigue or cognitive burden [31–33], the 36 paired comparisons in the experimental design were divided into four survey versions, each containing nine choice questions. Each physician was randomly assigned to one of the four versions and the order of the choice questions was randomized for each respondent. If physicians were assigned to the narrower cost range, the cost levels shown in the choice questions corresponded to the levels in the narrower range, and vice versa if physicians were assigned to the wider cost range. The risk-communication format did not affect the way information was presented in the choice questions or the experimental design. In each choice question, physicians were asked to indicate which of two hypothetical meningococcal vaccine profiles they would recommend for addition to the immunization schedule or whether they would not recommend either of the two alternative vaccines (Fig. 1). The survey also collected demographic information about the physicians.

Table 2 – Two risk-information formats.

Constant-base population information format

Out of 1 million children younger than 10 y:

- 333 are hospitalized for *head and neck injuries* each year
- 200 are diagnosed with *acute appendicitis* each year
- 15 are diagnosed with *acute myeloid leukemia (AML)* each year
- 11 are diagnosed with *meningococcal disease* each year (about the same number die from drowning each year)

Variable-base population information format

- 1 out of 3,000 children younger than 10 y is *hospitalized for head and neck injuries* each year. That is about the same as 1 child in a town with 20,000 residents.
- 1 out of 5,000 children younger than 10 y is diagnosed with *acute appendicitis* each year. That is about the same as 1 child in a town with 35,000 residents.
- 1 out of 65,000 children younger than 10 y is diagnosed with *AML* each year. That is about the same as 1 child in a city with 450,000 residents, such as Albuquerque, NM; Kansas City, MO; or Long Beach, CA.
- 1 out of 90,000 children younger than 10 y is diagnosed with meningococcal disease each year. That is about the same as 1 child in a city with 650,000 residents, such as Boston, MA; Memphis, TN; or Baltimore, MD. (About the same number of children younger than 10 y die from *drowning* each year.)

Study Sample

Physicians were recruited from the Physicians Consulting Network, a national online physician panel that verifies members' medical education with the American Medical Association. All participating physicians were board-eligible or board-certified pediatricians in the United States. The 20-minute online survey was administered in August 2011. Respondents were given a $55 cash honorarium if they completed at least one choice question in the survey. The Office of Research Protection and Ethics at Research Triangle Institute granted a consent exemption for this study.

Model and Analysis

In each choice question, we assume that the provider chose the vaccination (vaccine A, vaccine B, or neither) that provided the most subjective value, which is a form of the standard random utility model formulation [34]. In particular, we posit that the provider i's choice, $v_{i,k}^{*}$, is the solution to the following:

$$U_i(v_k) = \max U_i = \max \begin{cases} U_{i,k}(\mathrm{AGE}_k, \mathrm{EFF}_k, \mathrm{INJ}_k, \mathrm{VIS}_k, \mathrm{BST}_k, \mathrm{P}_k) \\ U_{i,k=0} \end{cases} \quad (1)$$

where v_k is the provider's choice; k denotes vaccine A, vaccine B, or the opt-out choice ($k = 0$); $U_{i,k}$ is the perceived value of vaccine

VACCINE FEATURE	VACCINE A	VACCINE B	
Age at which protection begins	4 months	2 years	
How well the vaccine protects against meningococcal disease	Prevents 350 cases of disease, 88 cases of disability, and 35 deaths over 5 years	Prevents 425 cases of disease, 110 cases of disability , and 43 deaths over 5 years	
Number of injections added to the schedule	2	4	
Number of additional visits required	3	None	
Need a booster vaccine after 5 years	No	Yes	
Total out of pocket cost to parents (for all meningococcal vaccine doses)	$75	$150	
If these were the only meningococcal vaccines available, which would you recommend be added to the vaccine schedule?	Vaccine A ○	Vaccine B ○	Neither ○

Fig. 1 – Example choice question. Before seeing the choice questions, respondents were shown the following text: "In this section, we will ask you to consider different possible meningococcal vaccines for infants. In each question, we will ask you to choose the vaccine that you think should be added to the vaccine schedule. All of the vaccines provide 5 years of protection from meningococcal disease and they all have the same, very low risk of side effects. They also have the same risk of mild side effects (such as injection-site reaction). These vaccines may be different than vaccines that are currently available or in development. Note that the addition of an infant meningococcal vaccine would not change the recommendation to vaccinate adolescents against meningococcal disease. It also would not affect the availability of meningococcal vaccines currently used to vaccinate adolescents and other individuals at risk of infection."

k to provider i, which depends on the vaccine characteristics, including the age at which protection begins (AGE), the vaccine effectiveness (EFF), the number of additional injections (INJ), the number of additional office visits (VIS), whether a booster vaccine is required (BST), and the cost (P); and $U_{i,k=0}$ is the perceived value of no vaccination.

To estimate the model, we assume that the provider's utility is a separable and linear function of the health outcomes and characteristics associated with each vaccine alternative, v_k. Equation 1 becomes

$$U_i(v_{k=A,B}) = \beta_{i,age}\mathrm{AGE}_k + \beta_{i,eff}\mathrm{EFF}_k + \beta_{i,inj}\mathrm{INJ}_k + \beta_{i,vis}\mathrm{VIS}_k + \beta_{i,bst}\mathrm{BST}_k + \beta_{i,\lambda}\mathrm{P}_k \quad (2)$$

$$U_i(v_{k=0}) = \beta_{i,opt}\mathrm{OPT} \quad (3)$$

where OPT is an effects-coded variable equal to 1 if the provider selected the opt-out alternative and equal to −1 otherwise.

The pattern of respondents' responses to the choice questions was analyzed using conditional logit and random-parameters logit (RPL) models. As shown in Equations 2 and 3, the dependent variable was discrete vaccine choice (or, recommendation), and the explanatory variables included effects-coded categorical variables describing the levels of the hypothetical vaccine attributes associated with the vaccines presented in the recommendation questions and an effects-coded variable indicating whether the respondent would recommend "neither" vaccine. To examine whether preferences for any vaccine features depended on the levels of other vaccine features, we included interactions between effects-coded variables. The i subscripts on the parameters measuring the marginal utility of the vaccine characteristics (β) indicate that all variables had random parameters with normal distributions in the RPL model. All analyses were conducted using NLOGIT 4.0, and the RPL models used 500 draws from the Halton sequence (Econometric Software, Inc., Plainview, NY).

The estimated parameters are log-odds preference estimates for the hypothetical vaccine attributes relative to the mean effect, normalized at zero. The estimates indicate the relative importance of each attribute level and can be interpreted in three ways [35–37]. First, the vertical distance between the importance weights for the best and worst levels of any attribute indicate the overall importance of that attribute over the range of levels included in the study relative to the importance of other attributes. Second, differences between adjacent importance weights indicate the relative importance of moving from one level of an attribute to an adjacent level of that attribute: the greater the difference, the more important the change from one level to the next. Third, the difference between adjacent importance weights of one attribute can be compared directly with the difference between adjacent importance weights of a different attribute.

The RPL parameter estimates were used to calculate both the percentage of respondents who would choose a hypothetical

infant meningococcal vaccine with given characteristics and the minimum acceptable efficacy (MAE). MAE is the smallest number of meningococcal disease cases prevented over 5 years necessary to compensate for an undesirable change in vaccine features. Similar to the maximum acceptable risk [38], the MAE is calculated as the ratio of the relative importance of a worsening in vaccine features divided by the relative importance of preventing a case of a meningococcal disease (efficacy).

The parameter estimates were combined with vaccine profiles in the experimental design to obtain a weighted, mean-value conjoint-utility index for the vaccine of interest. The conjoint-utility index was used to examine how the likelihood that one vaccine would be chosen over another vaccine (predicted choice probability) would change in response to changes in a single vaccine attribute, holding all other attributes constant as well as the probability of choosing vaccines with given profiles as a whole.

Results

Physician Sample Characteristics

Eleven hundred board-certified or board-eligible pediatricians were invited to participate. The e-mail invitation indicated that the survey was about vaccinations. Two hundred sixteen (19.6%) pediatricians agreed to participate (Table 3).

Two respondents always selected the same vaccine (either vaccine A or vaccine B) in the recommendation questions. These two respondents were deleted from the sample because this lack of variation suggested that these respondents did not pay attention to the recommendation questions. The final sample size used for analysis was 214.

Table 3 – Sample characteristics.

Characteristic	Frequency in sample (percentage of sample)
Sex	
Male	142 (65.7)
Female	74 (34.3)
Number of years in practice	
<1	0
1–3	2 (0.9)
4–6	9 (4.2)
7–9	20 (9.3)
10–15	52 (24.1)
16–20	43 (19.9)
21–25	36 (16.7)
>25	54 (25.0)
Type of practice	
Office-based private practice	185 (85.6)
Hospital-based private practice	14 (6.5)
Academic hospital-based practice	19 (8.8)
Other	8 (3.7)
Percentage of patients covered by*	
Medicaid	30.5 ± 25.7
Tricare insurance (for military families)	4.8 ± 8.1
Private insurance	59.2 ± 27.4
No insurance	5.5 ± 6.6
Treated a case of meningococcal disease	181 (83.8)
Offer the quadrivalent meningococcal conjugate vaccine (MCV4) to adolescents patients	211 (97.7)

* Values are mean ± SD.

Preferences for Vaccine Attributes

Initially, we estimated separate conditional logit models for the subsamples that saw the constant-base population risk-information format (n = 109) and the variable-base population risk-information format (n = 105) (see Table 4.) A Swait-Louviere test [39] indicated that the estimated parameters from these two models were quantitatively (and statistically) similar, meaning that physician preferences for hypothetical vaccine attributes did not vary with the risk-information format. The data from respondents considering the two different risk-information formats were pooled for the remaining analyses.

In addition, we estimated separate conditional logit models for the subsamples that saw the narrower cost range (n = 112) and the wider cost range (n = 102) (see Table 4). Figure 2 compares the importance weights for costs in these two subsamples. The distance between the best and worst levels of out-of-pocket costs to parents for the narrower cost range was 1.4 (= 0.5 – [–0.9]); the distance between the best and worst levels of out-of-pocket costs to parents for the much wider cost range was 1.7 (= 0.7 – [–1.0]). These relative differences are small compared with the large numeric differences in the ranges, and a *t* test indicated that they were not statistically different from one another ($P = 0.05$). The findings are consistent with respondents recoding the levels of parental cost as, for example, "none," "low," "medium," and "high," regardless of whether they were assigned to the narrower or wider cost range, rather than paying attention to the actual cost. These results suggest that the aggregate results did not pass this internal validity test. Furthermore, a Swait-Louviere test [39] indicated that the estimates were not statistically different in these two models. For all further analyses, we pooled the data from respondents considering the narrower cost range with the data from respondents considering the wider cost range.

An RPL model was estimated using the full data set. Table 5 and Figure 3 present the estimated log-odds preference estimates and 95% confidence intervals (CIs) for the five vaccine attributes relative to the mean effect, normalized at zero. The estimates are logically ordered. Respondents preferred protection at an earlier age, higher vaccine effectiveness, fewer additional injections and doctor's visits, and the absence of a required booster.

The models in Table 5 also show that physicians' preferences for the meningococcal vaccine effectiveness and the number of additional injections vary with the age at which protection begins. In particular, physicians place a lower weight on the highest level of protection (preventing 500 cases of disease) when the vaccine provides protection to the youngest age group; they place a higher weight on the same level of protection when the vaccine provides protection at age 12 months; and they place a higher weight on the three highest levels of protection when the vaccine provides protection to the oldest age group (24 months). In addition, physicians place a lower weight on the highest level of additional injections when protection is provided to the youngest age group and a higher weight on no additional injections if protection is not provided until 24 months. The statistically significant estimates of SD in Table 5 indicate the attribute levels for which there was heterogeneity in providers' preferences.

Note that Figure 3 presents the weights for only those levels of the age and visit attributes that correspond to features of actual candidate meningococcal vaccines (age 4 and 12 months, and 0

Table 4

A	B	C	D	E	F	G	H	I	J
Attribute	Level	Risk communication formats[a]				Cost Ranges[a]			
		Varying Numerator		Varying Denominator		Narrower		Wider	
		β	SE	β	SE	β	SE	β	SE
Age at which protection begins (months)	4	0.28***	0.07	0.55***	0.08	0.56***	0.08	0.28***	0.07
	12	0.05	0.07	-0.05	0.08	-0.14	0.08	0.12	0.07
	24	-0.33***	0.08	-0.50***	0.08	-0.43***	0.08	-0.40***	0.08
Number of cases of disease / disability / death prevented over five years	500/125/150	0.73***	0.10	0.74***	0.09	0.78***	0.10	0.68***	0.09
	425/110/43	0.28***	0.10	0.50***	0.10	0.46***	0.11	0.35***	0.10
	350/88/35	-0.37***	0.10	-0.41***	0.10	-0.49***	0.11	-0.29***	0.10
	250/63/25	-0.64***	0.10	-0.82***	0.11	-0.75***	0.12	-0.74***	0.10
Number of injections added to the schedule	0	0.33***	0.08	0.51***	0.08	0.44***	0.08	0.40***	0.08
	2	0.07	0.09	-0.15	0.09	-0.01	0.09	-0.03	0.09
	4	-0.40***	0.08	-0.36***	0.08	-0.43***	0.09	-0.38***	0.08
Number of additional visits required	0	0.19**	0.08	0.20**	0.08	0.27***	0.08	0.15**	0.08
	1	0.10	0.08	0.05	0.08	0.09	0.08	0.04	0.07
	3	-0.28***	0.07	-0.25***	0.07	-0.36***	0.07	-0.20***	0.07
Need a booster vaccine after 5 years	Yes	-0.10**	0.05	-0.06	0.06	-0.13**	0.06	-0.07	0.05
	No	0.10**	0.05	0.06	0.06	0.13**	0.06	0.07	0.05
Total out-of-pocket-cost to parents (for all vaccine doses)	$0	0.64***	0.09	0.65***	0.09	0.54***	0.09	0.70***	0.09
	$10 or $25	0.40***	0.11	0.35***	0.11	0.38***	0.12	0.45***	0.11
	$25 or $75	0.10	0.10	-0.28***	0.11	-0.06	0.10	-0.12	0.10
	$75 or $150	-1.13***	0.12	-0.73***	0.11	-0.87***	0.12	-1.03***	0.12
Interaction between protection at 4 mos and no. of cases prevented	4 mos X 500/125/150	-0.38**	0.18	-0.39**	0.19	-0.36	0.19	-0.38**	0.18
	4 mos X 425/110/43	0.19	0.20	0.05	0.19	0.33	0.22	-0.01	0.19
	4 mos X 350/88/35	-0.01	0.20	0.11	0.19	-0.14	0.21	0.17	0.19
	4 mos X 250/63/25	0.20	0.19	0.24	0.20	0.17	0.20	0.22	0.19
Interaction between protection at 12 mos and no. of cases prevented	12 mos X 500/125/150	0.35**	0.17	0.21	0.18	0.46**	0.18	0.11	0.17
	12 mos X 425/110/43	-0.15	0.20	-0.11	0.19	-0.36	0.20	0.01	0.19
	12 mos X 350/88/35	-0.03	0.18	0.09	0.18	0.10	0.19	-0.02	0.17
	12 mos X 250/63/25	-0.17	0.22	-0.20	0.22	-0.20	0.22	-0.10	0.22
Interaction between protection at 24 mos and no. of cases prevented	24 mos X 500/125/150	0.04	0.21	0.18	0.21	-0.10	0.22	0.27	0.20
	24 mos X 425/110/43	-0.04	0.17	0.06	0.17	0.03	0.18	0.00	0.17
	24 mos X 350/88/35	0.03	0.22	-0.20	0.22	0.04	0.22	-0.15	0.22
	24 mos X 250/63/25	-0.03	0.19	-0.04	0.19	0.03	0.19	-0.12	0.18
Interaction between protection at 4 mos and additional injections	4 mos X 0 additional injections	0.10	0.15	0.02	0.15	-0.17	0.15	0.22	0.15
	4 mos X 2 additional injections	0.24	0.15	0.13	0.15	0.32**	0.15	0.05	0.15
	4 mos X 4 additional injections	-0.34**	0.15	-0.15	0.15	-0.16	0.15	-0.27	0.14
Interaction between protection at 12 mos and additional injections	12 mos X 0 additional injections	-0.11	0.17	-0.05	0.17	0.01	0.17	-0.19	0.17
	12 mos X 2 additional injections	-0.10	0.17	-0.22	0.18	-0.23	0.17	-0.01	0.17
	12 mos X 4 additional injections	0.22	0.17	0.27	0.17	0.21	0.18	0.21	0.16

continued on next page

Interaction between protection at	**24 mos X 0 additional injections**	0.02	0.15	0.03	0.15	0.15	0.16	-0.02	0.15
24 mos and additional injections	**24 mos X 2 additional injections**	-0.14	0.17	0.09	0.17	-0.10	0.18	-0.04	0.16
	24 mos X 4 additional injections	0.12	0.15	-0.11	0.15	-0.05	0.16	0.06	0.15
Opt-out	Opt-out	-2.06***	0.15	-1.67***	0.13	-1.85***	0.15	-1.90***	0.14
Swait-Louviere Test Results	Estimated relative scale factor (95% confidence interval)	0.94 (0.82-1.06)				0.97 (0.84-1.09)			
	Likelihood ratio statistic for joint test of parameter equivalence (p-value)	32.6056 (0.11)				31.6268 (0.14)			

β = mean parameter estimates, or mean preference weight estimates; SE=standard error of parameter estimate; SD=Standard deviation of mean parameter. This is an estimate of the variability of or heterogeneity in the parameter estimate.

[a] The results reported in these columns are conditional logit model estimates.

and 1 additional visit, respectively). The vertical distance between importance weights indicates the relative importance of moving from one level of an attribute to another level of that attribute. For example, the relative importance of an improvement in vaccine effectiveness that increases the number of cases prevented from 250 to 350 was approximately 1.2 (= [–2.1] – [–0.9]). The relative importance of a change in the age at which protection begins from 4 to 12 months was approximately 0.7 (= 0.8 – 0.1). Therefore, an increase in the number of cases prevented from 250 to 350 was approximately 1.7 times as important as changing the age at which protection begins from 4 to 12 months. The same improvement in effectiveness was approximately 1.1 times as important as increasing the number of additional injections from 0 to 2 (1.1 = 1.10 – [–0.02]) and 8.3 times as important as increasing the number of doctor visits by 1 (0.1 = 0.5 – 0.4).

Given the attributes and levels used in the trade-off questions, respondents placed the greatest importance on improving effectiveness from preventing 250 cases to either 425 or 500 cases, improving effectiveness from preventing 350 cases to 500 cases, and increasing the number of additional injections required from 0 to 4. Respondents placed the smallest importance on the need for a booster vaccine.

The large negative preference estimate for the effects-coded opt-out variable indicates that respondents placed a very large weight on having an infant meningococcal vaccine in the vaccine schedule rather than not having one in the schedule. Most respondents (n = 171 or 79.9%) never selected the “no vaccine” option in the recommendation questions. Of the 1926 recommendation questions in the study, the no vaccine option was selected in 120 questions (6.2%). The results suggest that nearly all (99.96%; 95% CI 97%–100%) physicians in the sample would choose a vaccine with even the least-preferred vaccine features (i.e., protection begins at 12 months; 250 cases of disease, 63 cases of disability, and 25 deaths prevented; four injections added to the immunization schedule; one additional doctor’s visit required; no booster required; and an out-of-pocket cost of $150 to parents) rather than choose no infant meningococcal vaccine.

We estimated two additional models: 1) a main effects only RPL model and 2) an RPL model with the specification shown in Table 5 but estimated using 1000 Halton draws. The former results (not shown) indicated that the parameter estimates from the main effects only model were not statistically different from the main effects shown in Table 5. Furthermore, the parameter estimates based on the model using 1000 Halton draws (not shown) were not statistically different from the RPL parameters based on 500 Halton draws.

Table 6 presents selected MAE results. For example, to accept an increase in the age at which protection begins from 4 months to 12 months, respondents would require that the vaccine prevent an additional 31 cases of meningococcal disease over 5 years (95% CI 6.6–55.4). Respondents would require that more than three times as many additional cases of meningococcal disease be prevented over 5 years (100.7 cases; 95% CI 47.2–154.2) to accept an increase in additional injections from zero to four.

Given that more than one-half of respondents had at least 16 years of experience, we estimated separate conditional logit models for the two subsamples composed of respondents with at least 16 years of experience and less than 16 years of experience to examine whether physicians with more experience had preferences different from those of the remaining physicians. A Swait-Louviere test [39] indicated that the relative scale of the two models was different (estimated relative scale factor = 1.17; 95% CI 1.02–1.33). After accounting for the difference in scale, a likelihood-ratio test indicated that the preference weight estimates were not statistically different in these two groups (likelihood-ratio test statistic = 21.27; $P = 0.68$).

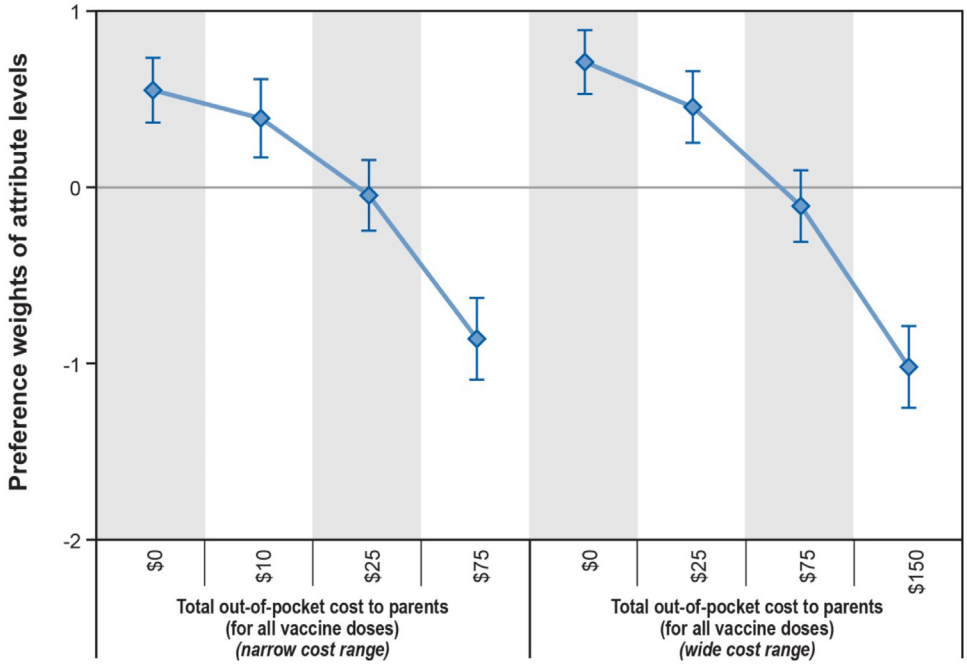


Fig. 2 – Estimated physicians' preference weights for total out-of-pocket costs, by cost range. Respondents were randomly assigned to one of the two cost ranges. The levels for parental costs in the narrow cost range were $0, $10, $25, and $75. The levels for parental costs in the wide cost range were $0, $25, $75, and $150.

Conclusions

In view of the fact that the ACIP has not endorsed universal infant meningococcal vaccination and it is unlikely that the Vaccines for Children program or private health insurance programs will cover the vaccine for children who are not at risk of meningococcal disease, the use of infant meningococcal vaccine by these families will depend on physicians' and parents' preferences for infant meningococcal vaccination. To our knowledge, these results provide the first systematic quantification of US pediatricians' subjective evaluation of the desirability of vaccinating infants up to age 12 months against meningococcal disease. When making decisions about licensing vaccines and recommending their use, the FDA's and ACIP's decisions are informed by the expert opinions of a limited number of empaneled physicians. In this study, we have surveyed a larger number of physicians and found that pediatricians place great importance on the vaccination of infants against meningococcal disease. Although this study does not rebut the cost-effectiveness findings with respect to infant meningococcal vaccination, it indicates the importance that pediatricians place on these vaccinations. Respondents' strong preference for adding a meningococcal vaccine for infants is reflected in the result that virtually all the physicians in the sample would choose a vaccine even if it had the least-preferred vaccine features rather than choose no infant meningococcal vaccine. Although our study did not directly address the difference between universal and permissive recommendations, the vaccine recommendation question asked physicians which vaccine they would recommend adding to the immunization schedule. Participants in the pretest understood that the hypothetical vaccine would be recommended for all children.

Second, the study indicates that pediatricians thought that some of the increases in vaccine effectiveness were among the most important factors in their vaccine recommendations, followed by some of the increases in the number of injections. Whether a booster was required after 5 years was the least important factor in vaccine recommendations. The results show that physicians reacted logically to higher prices (preference weights declined as cost increased), but they generally were insensitive to the absolute level of prices parents would have to pay. Third, the MAE estimates implied that vaccines that require additional injections would require a larger increase in efficacy to offset the undesirable change that would be required to compensate for changes in age at which protection begins or the number of additional office visits.

Although there have been no previous studies of physicians' preferences for meningococcal vaccines, health care providers participated in four public Centers for Disease Control and Prevention (CDC) meetings discussing the vaccination of infants and toddlers against meningococcal disease [40]. The DCE study results reported in this article provide quantitative evidence to support the qualitative data on provider attitudes reported by the CDC. For example, Nowak [40] reported that some health care providers attending the CDC-sponsored public meetings were concerned about adding vaccines to an already crowded vaccine schedule [40]. This is reflected in the fact that the second most important vaccine attribute in this study was the number of vaccines added to the immunization schedule. Furthermore, the results reported in this article are similar to the results of an unpublished survey of health care providers [40] that indicated that 90% of the providers would recommend infant meningococcal vaccination to parents if the ACIP endorsed universal immunization and there were no additional injections required. The results also indicated that providers' willingness to recommend the vaccine to parents would decline if the ACIP did not endorse universal immunization, or the number of injections increases, or a vaccine would require a change in the use of other vaccine products. Although the DCE study asked about physicians' willingness to recommend adding a vaccine to the immunization schedule, rather than their willingness to recommend a vaccine to parents, the DCE study results are qualitatively similar to the results of the unpublished physician survey [41]. Both our study

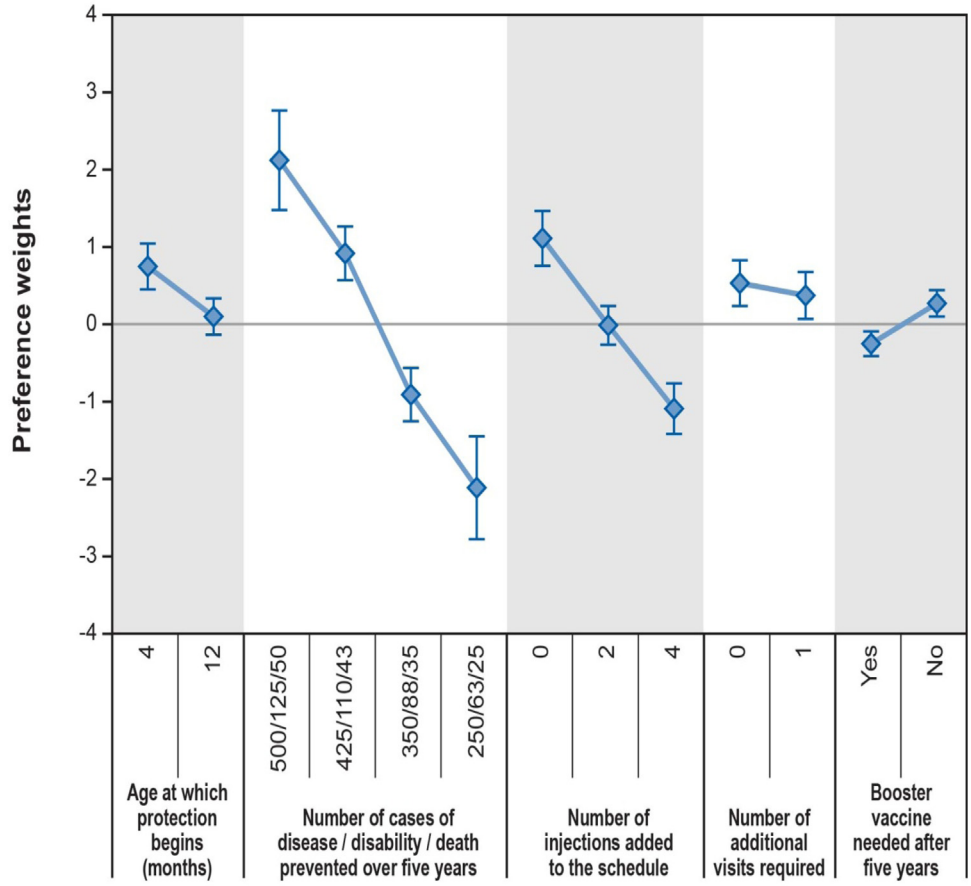
Table 5

A	B	K	L	M
Attribute	Level	RP Logit		
		β	SE	SD
Age at which protection begins (months)	4	0.76***	0.15	1.56***
	12	0.09	0.11	0.56***
	24	-0.84***	0.17	Omitted
Number of cases of disease / disability / death prevented over five years	500/125/150	2.12***	0.33	1.51***
	425/110/43	0.91***	0.18	0.08
	350/88/35	-0.91***	0.18	0.23
	250/63/25	-2.12***	0.34	omitted
Number of injections added to the schedule	0	1.10***	0.18	0.55***
	2	-0.02	0.13	0.18
	4	-1.08***	0.17	omitted
Number of additional visits required	0	0.52***	0.15	0.70***
	1	0.38**	0.16	0.37**
	3	-0.90***	0.18	Omitted
Need a booster vaccine after 5 years	Yes	-0.26***	0.09	0.20
	No	0.26***	0.08	Omitted
Total out-of-pocket-cost to parents (for all vaccine doses)	$0	1.79***	0.30	1.71***
	$10 or $25	1.16***	0.25	1.54***
	$25 or $75	-0.01	0.16	0.79***
	$75 or $150	-2.94***	0.47	Omitted
Interaction between protection at 4 mos and no. of cases prevented	**4 mos X 500/125/150**	-0.76**	0.30	1.36***
	4 mos X 425/110/43	-0.01	0.30	0.82***
	4 mos X 350/88/35	0.41	0.30	0.45
	4 mos X 250/63/25	0.22	0.19	Omitted
Interaction between protection at 12 mos and no. of cases prevented	**12 mos X 500/125/150**	0.64**	0.31	0.83***
	12 mos X 425/110/43	-0.25	0.31	0.57**
	12 mos X 350/88/35	-0.35	0.27	0.56
	12 mos X 250/63/25	-0.04	0.36	Omitted
Interaction between protection at 24 mos and no. of cases prevented	**24 mos X 500/125/150**	0.12***	0.34	Omitted
	24 mos X 425/110/43	0.26***	0.26	Omitted
	24 mos X 350/88/35	-0.06***	0.32	Omitted
	24 mos X 250/63/25	-0.32	0.32	Omitted
Interaction between protection at 4 mos and additional injections	**4 mos X 0 additional injections**	-0.17	0.24	0.37
	4 mos X 2 additional injections	0.49**	0.22	0.73**
	4 mos X 4 additional injections	-0.32	0.23	Omitted
Interaction between protection at 12 mos and additional injections	**12 mos X 0 additional injections**	0.09	0.27	0.03
	12 mos X 2 additional injections	-0.24	0.26	1.30***
	12 mos X 4 additional injections	0.15	0.28	Omitted
Interaction between protection at 24 mos and additional injections	**24 mos X 0 additional injections**	0.07***	0.24	Omitted
	24 mos X 2 additional injections	-0.25	0.26	Omitted
	24 mos X 4 additional injections	0.18	0.27	Omitted
Opt-out	Opt-out	-7.53***	1.30	5.44***
Swait-Louviere Test Results	Estimated relative scale factor (95% confidence interval)	N/A		
	Likelihood ratio statistic for joint test of parameter equivalence (p-value)	N/A		

β = mean parameter estimates, or mean preference weight estimates; SE=standard error of parameter estimate; SD=Standard deviation of mean parameter. This is an estimate of the variability of or heterogeneity in the parameter estimate; N/A=not applicable

and the unpublished physician survey [41] indicate strong support for vaccination despite the low incidence of the disease and the fact that infant meningococcal vaccination is not cost-effective. It is not clear from either study why physicians place such importance on infant meningococcal vaccination, but several pretest respondents in the present study stated that they are very concerned about misdiagnosing the disease or otherwise having their patients experience severe meningococcal disease outcomes. These concerns may cause respondents to inflate the small disease risks. The only previous study of preferences for meningococcal vaccination was undertaken by Bishai et al. [11]. The study elicited German and French parents' preferences and willingness to pay for adolescent meningococcal vaccines. As in our study, most respondents in the Bishai et al. [11] study (93%) indicated that they would purchase a vaccine if it was not free. The study results indicated that the uptake of a quadrivalent meningococcal vaccine that lasted 10 years would be 50% in France and Germany at prices of €80 and €50, respectively.

Our risk-communication experiment found that preferences for infant meningococcal vaccines did not vary with different risk-information formats. This result contrasts with previous findings for nonphysicians that people often focus on fraction



Brackets indicate 95% confidence intervals.

Fig. 3 – Physician preference weights for features of infant meningococcal vaccines, parameter log odds relative to mean effect.

numerators and pay less attention to denominators in probability assessments [2]. Experts may make fewer errors in decision making if their processing of risk information improves as expertise develops [42].

Despite the increasing use of DCE in health applications to elicit preferences [15,43,44], this approach has several potential limitations. One inherent limitation is that the physicians evaluated hypothetical vaccine profiles that do not have the same significance as recommendations involving actual vaccines. We minimized the potential for hypothetical bias by offering vaccines that mimic real-world trade-offs as closely as possible. Furthermore, physicians' actual vaccine choices may differ from predicted choices because actual choices depend on a number of clinical, institutional, and financial factors that are beyond the scope of this study. One of the key issues in the real-world policy discussion about infant meningococcal vaccines is the breadth of protection provided by available vaccines. Our study did not disclose whether the hypothetical vaccines were bivalent or quadrivalent. Rather, it presented hypothetical effectiveness levels that varied over a range consistent with protection against different serogroups. Given the estimated annual burden of disease reported in Cohn et al. [3], the range of vaccine effectiveness shown in the DCE study (described in terms of the number of cases prevented over 5 years) would be approximately

Table 6 – Minimum acceptable efficacy (additional cases of meningococcal disease prevented over 5 years) in exchange for changes in vaccine features.

Change in Vaccine Features		Mean Minimum Acceptable Efficacy	95% Confidence Interval
Increasing the age at which protection begins from 4 to 12 months		31	7- 55
Increasing the number of additional injections required from	0 to 4 injections	101	47-154
	2 to 4 injections	49	17-81
	0 to 2 injections	52	19-85
Increasing the number additional doctor's visits from 0 to 1 visit		7	−12-25
Changing requirement for booster from no booster to booster required after 5 years		24	3-46

equivalent to bivalent and quadrivalent infant meningococcal vaccines that would be approximately 33% to 66% and 25% to 50% effective, respectively. Also, although vaccine safety was not included as an attribute because there have been no significant safety problems associated with meningococcal vaccines, respondents were asked to assume that all the hypothetical vaccines described in the survey had the same risk of mild side effects, such as injection-site reactions.

Furthermore, as in any survey-research study, we need to be mindful of sample representativeness as a potential study limitation. Although the sampling procedure was not inherently biased, the sample was small relative to the population. We cannot fully judge how representative our pediatrician sample was or whether our results are generalizable to all US pediatricians.

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