



# Societal Preferences for Meningococcal B Vaccination in Children: A Discrete Choice Experiment in Spain

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Received: August 3, 2022 / Accepted: September 27, 2022 / Published online: November 11, 2022  
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## ABSTRACT

**Introduction:** Immunization is the most effective strategy for the prevention of invasive meningococcal disease caused by *Neisseria meningitidis* serogroup B (MenB); however, parents need to weigh the risk–benefit and financial impact of immunizing their children

against MenB in the absence of a national immunization program (NIP). This study aimed to explore societal preferences (of parents and pediatricians) regarding the attributes of a MenB vaccine in Spain.

**Methods:** A discrete choice experiment (DCE) based on cross-sectional surveys was carried out to determine preferences. A literature review and scientific committee determined the six attributes related to the MenB vaccine included in the DCE: vaccination age, cost, duration, percentage of protection, adverse events probability, and expert/authority recommendation.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s40121-022-00708-7>.

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Data were analyzed using a mixed logit model. Relative importance (RI) of attributes was calculated and compared between parents and pediatricians.

**Results:** A total of 278 parents [55.8% female, mean age 40.4 (standard deviation, SD 7.3) years] and 200 pediatricians [73.0% female, mean age 45.8 (SD 12.9) years] answered the DCE. For parents, the highest RI was attributed to vaccine cost, expert/authority recommendation, and percentage of protection (26.4%, 26.1%, and 22.9%, respectively), while for pediatricians the highest RI was assigned to percentage of protection, expert/authority recommendation, and vaccination age (27.2%, 23.7%, and 22.6%, respectively). Significant

differences between parents and pediatricians were found in the RI assigned to all attributes ( $p < 0.001$ ), except for vaccine recommendation.

**Conclusion:** In the decision regarding MenB vaccination, cost was a driver in parental decision-making but had a low RI for pediatricians and, conversely, vaccination age was highly valued by pediatricians but was the attribute with least importance for parents. Despite these differences, expert/authority recommendation and percentage of protection were essential criteria for both groups. These results provide relevant information about MenB vaccination, highlighting the importance of considering societal preferences for NIP inclusion.

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Graphical Abstract:

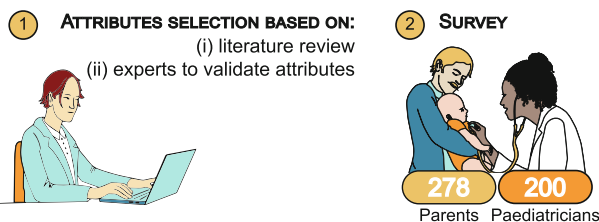
### SOCIETAL PREFERENCES FOR MENINGOCOCCAL B VACCINATION IN CHILDREN: A DISCRETE-CHOICE EXPERIMENT IN SPAIN

F. Martín-Torres, Á. Gil de Miguel, J. Ruiz-Contreras, L.A. Vallejo-Aparicio, A. García, M.C. Gonzalez-Inchausti, E. de Gomensoro, Z. Kocaata, C. Gabás-Rivera, M. Comellas, M. Prades, L. Lizán

-  *Neisseria meningitidis* serogroup B (MenB) is the most common cause of bacterial meningitis in many industrialized countries.
-  Most cases occur in children, with infants less than 1 year of age being the most frequently affected.
-  It can be effectively prevented by vaccination.

In absence of a National Immunization Program in Spain, the risk-benefit and financial impact of immunizing children against MenB needs to be weighted.

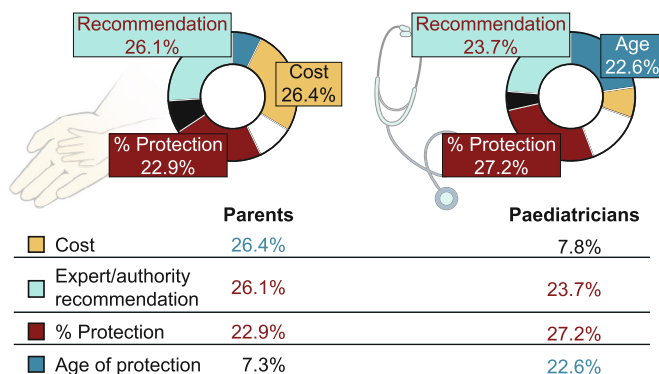
THE STUDY explored societal preferences (represented by parents and paediatricians) regarding six attributes of a MenB vaccine through a Discrete Choice Experiment\*.



SIX ATTRIBUTES

-  Age of protection
-  Cost
-  Duration of protection
-  Percentage of protection
-  Adverse events
-  Expert/Authority recommendations

WHAT PARENTS AND PAEDIATRICIANS VALUE MOST



Expert recommendation and percentage of protection were essential attributes for both groups.

Considering the preferences of key social segments is critical when including new vaccines in National Immunization Programs.

\*This methodology, aimed here at assessing individual preferences for MenB vaccine, is based on the premise that medical interventions can be described as combinations of different attributes

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**Keywords:** Children; Discrete-choice experiment; Meningococcal disease; Meningococcus B; *Neisseria meningitidis*; Pediatric; Preferences; Serogroup B; Vaccination; Vaccine

### Key Summary Points

#### *Why carry out this study?*

In the absence of a national immunization program (NIP) recommendation, the risk–benefit and financial impact of immunizing children against meningococcal disease caused by *Neisseria meningitidis* serogroup B (MenB) needs to be weighed.

This study explored societal preferences (represented by parents and pediatricians) regarding the attributes of a MenB vaccine in Spain.

#### *What was learned from the study?*

Expert/authority recommendation and percentage of protection were essential criteria for both parents and pediatricians.

Vaccine cost was a driver in decision-making of parents but not of pediatricians, while vaccination age was highly valued by pediatricians but not by parents.

Results highlight the importance of considering societal preferences for NIP inclusion of MenB vaccine.

## DIGITAL FEATURES

This article is published with digital features, including a graphical abstract, to facilitate understanding of the article. To view digital features for this article go to <https://doi.org/10.6084/m9.figshare.21215567>.

## INTRODUCTION

*Neisseria meningitidis* serogroup B (MenB) is the most common cause of bacterial meningitis in many industrialized countries [1]. Most cases occur in children [2], with infants less than 1 year of age being the most frequently affected [1]. In this age group, MenB has one of the highest case fatality rates (5–6%) of any bacterial infection [3]. Of patients that survive, 30–40% develop debilitating sequelae, which may include limb amputation, hearing loss, skin scarring, and chronic headaches [4].

Immunization is the most effective strategy for the prevention of meningococcal disease [5], and good safety profile of the universal mass vaccination has been demonstrated [6]. Two recombinant vaccines against MenB are available (4CMenB, Bexsero, GSK; and MenB-fHbp, Trumenba, Pfizer) [7, 8], whether for private purchase in several countries or through publicly funded national immunization programs (NIPs) in countries such as Czech Republic, Ireland, Italy, Lithuania, Malta, Portugal [9], and the UK [10]. While the Spanish Association of Pediatrics has been advocating for it since 2014 [8], vaccination against MenB is not yet part of the NIP in Spain. However, it is funded by several autonomous regions, including the Canary Islands, Castilla y León, and, most recently, Catalonia, Andalucía [8], and Galicia [11].

Uptake of an available MenB vaccine on the private market is likely influenced by perceived potential benefits, including protection against disease, and risks, such as potential side effects [5]. Therefore, parents need to weigh up the risk–benefit and financial impact of their decision to have their child immunized against MenB disease or not [12].

Understanding how patients and other stakeholders value many aspects of a healthcare intervention is vital to both the design and evaluation of such a program. Incorporating these values in decision-making may ultimately result in clinical, licensing, reimbursement, and policy decisions that better reflect the preferences of stakeholders and society, especially patients [13].

In this context, it is important to gain insight into vaccine-related behavior, including attitudes and preferences of parents and healthcare professionals for vaccines, and thereby identify key factors associated with the decision to vaccinate children or not. Community views and preferences can be measured by applying methodologies designed for choice assessment, such as the discrete choice experiment (DCE). This methodology has been increasingly applied to identify preferences for vaccines and vaccination programs, revealing substantial heterogeneity of findings [14–19]. DCEs rely on individual knowledge or perceptions of one's preferences, and on the ability to make trade offs between alternatives in the case of constraints such as money, time, availability, and others [20]. In comparison with other survey methods, it may be argued that a DCE more closely resembles real-world decision processes [21].

By exploring the preferences of Spanish society, represented by parents and pediatricians, regarding the attributes or characteristics of a MenB vaccine, the present study aimed to provide insights into determinants of vaccination choice and relevant attributes for the inclusion of MenB vaccine in the NIP.

## METHODS

### Study Design and Participants

To compare preferences between groups and detect significant differences, Orme recommends using a sample size of at least 200 per group [22]. Following that recommendation, a target sample of 200 parents of children aged 0–14 years and 200 pediatricians was considered. These groups were considered to be representative of Spanish society. Additionally, it was confirmed that this sample size would have sufficient statistical power (80% and 90%, respectively) to reveal differences between groups (should they exist). Different sample sizes were estimated using the comparison of proportions approach and hypothetical mean differences of relative importance (RI) (from 1 to 10 points) and standard deviations (SD)

(Supplementary Table S1). The resulting sample sizes were under 200 per group.

The market research company Growth for Knowledge (GfK) recruited parents through an online panel. They needed to have at least one child (0–14 years), to understand the Spanish language, and to have lived in Spain for at least 10 years (considered an appropriate minimum period to get to know the Spanish language, culture, and healthcare system enough to understand the study questionnaire). The invitation of pediatricians was performed through the Spanish Society of Hospital and Primary Care Pediatricians. Parents and pediatricians voluntarily accepted to participate in the study. The study questionnaire was available from September to October 2021.

The survey enrollment was stratified approximately 50/50 by gender, children's age [having an infant (0–2 years) or not] and educational level [low (primary or secondary education)/high (vocational or university education)], to ensure adequacy for the study aims and generalizability to the Spanish population.

The study was evaluated by the Ethics Committee of the Hospital Universitario Puerta de Hierro (Madrid), which considered that there was no ethical or legal impediment to its realization. The study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. No economic compensation was offered to participants.

A steering committee consisting of two pediatricians and one expert in public health led the study. The steering committee guided the study's development, validated and selected which attributes and levels should be included in the DCE, and reviewed all study documents.

### DCE Methodology

This methodology, aimed at assessing individual preferences for MenB vaccine, is based on the premise that medical interventions can be described as combinations of different attributes. DCE involves asking respondents to choose between competing scenarios, each comparing two hypothetical treatment options

with a series of defined attributes represented at various levels (e.g., an attribute of “route of administration” at the level of “oral”). The value that individuals attach to their constituent parts is then derived via probabilistic choice models [23]. The design and analysis of the present study are in accordance with the checklist and reports of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Conjoint Analysis Task Forces [13, 24, 25].

### Attributes and Levels Selection

The selection of attributes and levels related to MenB vaccine was based on a literature review of previous DCE studies on vaccination, and subsequently on a focus group among experts in the field (scientific committee). For the literature review, key terms related to vaccination and methods for assessing preferences were used to search the PubMed/MEDLINE database (Supplementary Table S2). Studies assessing preferences for pediatric vaccine attributes, published from 12 March 2011 to 12 March 2021, were reviewed. A total of 20 studies with potential attributes for inclusion in the DCE were identified.

The main purposes of the focus group were, first, to validate the potential attributes found in the literature; second, to identify relevant attributes not retrieved; and third, to assess the comprehensibility of the attributes and levels proposed. Six attributes, with a maximum of three levels each, were selected (Table 1).

### Survey Instrument and Experimental Design

A web-based survey was completed by parents and pediatricians. The survey included sociodemographic data and the choice tasks (Supplementary Table S3).

An experimental design was constructed, which consisted of a series of choice tasks from combinations of the attribute levels (called scenario alternatives). An orthogonal factorial design generated 18 scenarios through a mix-and-match algorithm used to generate the choice sets for presentation. These 18 scenarios were divided into two blocks, each containing nine pairwise choice sets to reduce the size of

**Table 1** Attributes and levels considered in the discrete choice experiment

Attributes	Levels
Cost	0 (100% State)
	€150 (vaccine with prescription, of which family pays €150, and State pays €150)
	€300 (100% family)
Efficacy/effectiveness	3 years (requires booster dose after 3 years)
	10 years (requires booster dose after 10 years)
	Lifetime (no booster dose required)
	90% (prevents 9 out of 10 MenB infections)
Common adverse events	70% (prevents 7 out of 10 MenB infections)
	50% (prevents 5 out of 10 MenB infections)
	10%
Recommendation	25%
	50%
	No recommendation
Vaccination age	Scientific societies
	Scientific societies and health authorities
Vaccination age	At any age (from 2 months)
	From 10 years of age

*MenB Neisseria meningitidis* serogroup B

the questionnaire presented to participants. Within each block, a first-choice scenario (pair one out of ten) with dominant options was added, as generally performed in DCEs [26]. This scenario was clearly superior and was therefore the chosen option, and thus was used to test if respondents made rational choices throughout the experiment. Data of those respondents who failed these rationality tests



**Table 2** Example of a choice set presented to the study participants

	Vaccine A	Vaccine B
Age at which vaccination is indicated	From 10 years old	From 10 years old
Cost of initial vaccine (three doses) assumed by the family	€0 (100% covered by State)	€150 (vaccine with prescription, of which family pays €150 and State €150)
Duration of protection against MenB after initial regimen (and need for additional doses to maintain protection)	Lifetime (no booster vaccine required)	10 years (requires booster vaccine after 10 years)
Percentage of protection against MenB	70% (prevents 7 out of 10 MenB infections)	70% (prevents 7 out of 10 MenB infections)
Likelihood of common adverse effects (local pain, fever, etc.) associated with the vaccine	25%	25%
Vaccine recommended by...	No recommendation	Scientific societies
	I prefer A <input type="checkbox"/>	I prefer B <input type="checkbox"/>

*MenB Neisseria meningitidis* serogroup B

were excluded from the final analysis. Table 2 shows an example of the choice set.

A pilot study comprising 13 parents of children aged 0–14 years and six pediatricians was initially completed in July–August 2021, to ensure clarity and feasibility of the survey content.

### Statistical Methods

Sociodemographic variables were described using relative and absolute frequencies of response for qualitative variables, while quantitative variables were described using statistics of centrality and dispersion.

To assess the preference value attributed to the characteristics of a MenB vaccine, the responses given to the DCE choice set by each group (parents and pediatricians) were analyzed using a mixed logit model, which accounted for preference heterogeneity [25]. Among the six included DCE attributes, cost was coded as a continuous quantitative variable (the utility value for the unit was obtained), to allow for the estimation of the willingness to pay (WTP)/monetary valuation of the benefits provided by the vaccine. Note that, for pediatricians, cost was considered as the monetary valuation of the benefits provided by the vaccine, assessing their altruistic preference, rather than actual WTP. All other attributes were considered qualitative for the analysis.

The regression coefficients obtained from the mixed logit model, referred to as partial utilities, were interpreted as the utilities associated with each level within an attribute. These coefficients were not directly comparable between attributes. To this end, the RI of an attribute over the range of attributes included in the experiment was estimated for each participant. It is defined as the range of partial utilities of an attribute (difference in partial utilities between the best/preferred level and the worst/least-preferred level of the same attribute), divided by the sum of all ranges across attributes, multiplied by 100. The mean RI of each attribute was calculated for each group of participants (parents and pediatricians). Furthermore, to assess differences and similarities between parents' and pediatricians' preferences, individual RIs between groups were compared using

comparisons of means (*t*-tests) or equivalent nonparametric tests (Mann–Whitney *U* tests).

To identify possible explanatory variables of parents' and pediatricians' preferences, a step-wise multiple regression analysis (beta regression) was performed for the RI of each attribute. The values of RI were considered as the dependent variable, and the sociodemographic variables as the independent ones. For parents, the following sociodemographic variables were considered: gender (male versus female), age (numerical, no subgroups), having children (aged 0–2 versus > 2–14 years), residence (urban versus rural), previous knowledge about MenB disease (yes versus no), educational level [low versus high (university or higher)], and monthly household income (< €3,000 versus ≥ €3,000; < €3,000 versus "I prefer not to answer"). For pediatricians, age and time of professional experience were considered (both numerical, no subgroups).

Finally, WTP/monetary valuation for a given clinical benefit [increased duration or percentage of protection, or reduced likelihood of adverse events (AEs)] was estimated as the ratio of the partial utility of the attribute levels and the partial utility of the cost [27].

## RESULTS

### Sociodemographic Characteristics of Participants

A total of 278 parents [55.8% female, mean age 40.4 (SD 7.3) years] and 200 pediatricians [73.0% female, mean age 45.8 (SD 12.9) years] answered the study survey (Table 3).

### Preferences for Attributes

All items were found to be statistically significant ( $p < 0.05$ ) in both parents' and pediatricians' preferences, except for a 50% probability of AEs (Table 4). Participants were more likely to choose a vaccine that could be administered at younger ages and had a lower cost, higher duration, and percentage of protection, with lower probability of AEs and recommended by

**Table 3** Sociodemographic characteristics of participants

Variable	Value
(A) Parents	
Female, <i>n</i> (%)	155 (55.8)
Age (years), mean (SD)	40.4 (7.3)
Having children 0–2 years, <i>n</i> (%)	128 (46.0)
Having children > 2–14 years, <i>n</i> (%)	246 (88.5)
Having children > 14 years, <i>n</i> (%)	57 (20.5)
Autonomous region, <i>n</i> (%)	
Andalucía	50 (18.0)
Aragón	17 (6.1)
Principado de Asturias	4 (1.4)
Islas Baleares	5 (1.8)
Canarias	5 (1.8)
Cantabria	6 (2.2)
Castilla y León	19 (6.8)
Castilla-La Mancha	14 (5.0)
Cataluña	38 (13.7)
Comunidad Valenciana	40 (14.4)
Extremadura	7 (2.5)
Galicia	8 (2.9)
Comunidad de Madrid	43 (15.5)
Región de Murcia	6 (2.2)
Comunidad Foral de Navarra	4 (1.4)
País Vasco	10 (3.6)
La Rioja	1 (0.4)
Ciudad Autónoma de Melilla	1 (0.4)
Residence, <i>n</i> (%)	
Rural (< 10,000 inhabitants)	42 (15.1)
Urban (> 10,000 inhabitants)	236 (84.9)
Educational level, <i>n</i> (%)	



**Table 3** continued

Variable	Value
Primary education	6 (2.2)
Secondary education	56 (20.1)
Vocational education	63 (22.7)
University education	153 (55.0)
Marital status, <i>n</i> (%)	
Single	9 (3.2)
Married or cohabiting	252 (90.6)
Separated or divorced	16 (5.8)
Other	1 (0.4)
Monthly household income, <i>n</i> (%)	
< €1,000	9 (3.2)
€1000–3000	176 (63.3)
€3000–6000	66 (23.7)
> €6000	2 (0.7)
I prefer not to answer	25 (9.0)
Prior knowledge about meningococcal disease (from relatives, friends, media, etc.), <i>n</i> (%)	245 (88.1)
(B) Pediatricians	
Female, <i>n</i> (%)	146 (73.0)
Age (years), mean (SD)	45.8 (12.9)
Time of professional experience, years (SD)	18.7 (12.0)
Autonomous region, <i>n</i> (%)	
Andalucía	30 (15.0)
Aragón	5 (2.5)
Principado de Asturias	9 (4.5)
Illes Balears	9 (4.5)
Canarias	1 (0.5)
Cantabria	5 (2.5)

**Table 3** continued

Variable	Value
Castilla y León	17 (8.5)
Castilla-La Mancha	15 (7.5)
Cataluña	29 (14.5)
Comunidad Valenciana	22 (11.0)
Extremadura	6 (3.0)
Galicia	24 (12.0)
Comunidad de Madrid	3 (1.5)
Región de Murcia	11 (5.5)
Comunidad Foral de Navarra	5 (2.5)
País Vasco	9 (4.5)
Residence, <i>n</i> (%)	
Rural (< 10,000 inhabitants)	40 (20.0)
Urban (> 10,000 inhabitants)	160 (80.0)
Type of practice, <i>n</i> (%)	
Public	179 (89.5)
Private	54 (27.0)

*n* number, *SD* standard deviation

different organizations (experts/health authorities).

Among all the attributes studied, parents assigned the highest RI to vaccine cost (RI 26.4%), followed by expert/authority recommendation (RI 26.1%), and percentage of protection (RI 22.9%), while for pediatricians the highest RI was assigned to percentage of protection (RI 27.2%), then expert/authority recommendation (RI 23.7%), and vaccination age (RI 22.6%). Significant differences were found in the RI assigned to all attributes ( $p < 0.001$ ) between parents and pediatricians, except for vaccine recommendation (Fig. 1).

**Table 4** Utility scores from the mixed logit model in parents and pediatricians

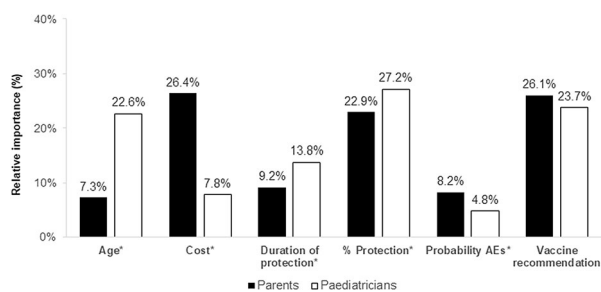
Attribute	Levels	Coefficient (partial utilities)	Standard error	p-Value
(A) Parents				
Age	At any age (from 2 months) <sup>a</sup>	0	–	–
	From the age of 10 years	–0.3620	0.1135	<b>0.0010*</b>
Cost	Per unit (€1) <sup>a</sup>	–0.0039	0.0005	<b>&lt; 0.0001*</b>
	€0 (100% State)	0	–	–
	€150 (vaccination with prescription, of which €150 family, €150 State)	–0.5838	–	–
	€300 (100% family)	–1.1676	–	–
Duration of protection	Lifetime (no booster vaccination required) <sup>a</sup>	0	–	–
	10 years (requires booster vaccination every 10 years)	–0.4513	0.1144	<b>&lt; 0.0001*</b>
	3 years (requires booster vaccination every 3 years)	–0.4536	0.9538	<b>&lt; 0.0001*</b>
Percentage of protection	90% <sup>a</sup>	0	–	–
	70%	–0.7389	0.1146	<b>&lt; 0.0001*</b>
	50%	–1.1116	0.1428	<b>&lt; 0.0001*</b>
Probability of common adverse events	10% <sup>a</sup>	0	–	–
	25%	–0.3971	0.1250	<b>0.0010*</b>
	50%	–0.2338	0.1248	0.0610
Vaccine recommendation	Scientific societies and health authorities <sup>a</sup>	0	–	–
	Scientific societies	–0.5477	0.9076	<b>&lt; 0.0001*</b>
	No recommendation	–1.1539	0.1209	<b>&lt; 0.0001*</b>
(B) Pediatricians				
Age	At any age (from 2 months) <sup>a</sup>	0	–	–
	From the age of 10 years	–2.7480	0.3132	<b>&lt; 0.0001*</b>
Cost	Per unit (€1) <sup>a</sup>	–0.0028	0.0005	<b>&lt; 0.0001*</b>
	€0 (100% state)	0	–	–
	€150 (vaccination with prescription, of which €150 family, €150 state)	–0.4201	–	–
	€300 (100% family)	–0.8402	–	–

**Table 4** continued

Attribute	Levels	Coefficient (partial utilities)	Standard error	p-Value
Duration of protection	Lifetime (no booster vaccination required) <sup>a</sup>	0	–	–
	10 years (requires booster vaccination every 10 years)	–1.3909	0.1862	< 0.0001*
	3 years (requires booster vaccination every 3 years)	–1.5881	0.1876	< 0.0001*
Percentage of protection	90% <sup>a</sup>	0	–	–
	70%	–2.0148	0.2363	< 0.0001*
	50%	–3.1469	0.3462	< 0.0001*
Probability of common adverse events	10% <sup>a</sup>	0	–	–
	25%	–0.5361	0.1902	0.0050*
	50%	–0.3494	0.2141	0.1030
Vaccine recommendation	Scientific societies and health authorities <sup>a</sup>	0	–	–
	Scientific societies	–0.9048	0.1587	< 0.0001*
	No recommendation	–2.7713	0.2483	< 0.0001*

<sup>a</sup>Reference value

\*Significant attribute level, p-value < 0.05. The sign of the coefficient indicates the sense of preference preferences (higher value, higher preference)



**Fig. 1** Parents’ and pediatricians’ relative importance. \*p-value < 0.001; AEs adverse events

**Determinants of Preferences**

According to the multiple regression results, parents’ preference (RI) for the attributes considered in the DCE could be explained by

several variables (Table 5), with household income being the most influential variable. Parents with monthly household income ≥ 3000 assigned higher RI to vaccination age, duration of protection, and probability of AEs, and lower RI to cost (as compared with parents with monthly household income < €3000). Additionally, older parents attributed higher RI to the age of vaccine administration, and lower RI to the percentage of protection. Parents having children aged 0–2 years assigned a higher RI to age and duration of protection than those not having children in this age group, while mothers assigned less RI to the cost of the vaccine and higher RI to the expert/authority recommendation than fathers. Finally, parents with prior knowledge of the disease assigned a higher RI to the percentage of protection than those without. However, pediatricians’ preferences were not explained by the variables

**Table 5** Parents' significant variables in the regression analysis

RI	Variable	Coefficient	SD	p-Value
Vaccination age	Age	0.009	0.004	0.035*
	Without a child aged 0–2 years <sup>a</sup>	0	–	–
	With a child aged 0–2 years	0.140	0.061	0.021*
	Monthly household income < €3000 <sup>a</sup>	0	–	–
	Monthly household income ≥ €3000	0.140	0.062	0.023*
Cost	Gender male <sup>a</sup>	0	–	–
	Gender female	–0.241	0.114	0.034*
	Monthly household income < €3000 <sup>a</sup>	0	–	–
	Monthly household income ≥ €3000	–0.349	0.134	0.009*
Duration of protection	Without a child aged 0–2 years <sup>a</sup>	0	–	–
	With a child aged 0–2 years	0.069	0.032	0.033*
	Monthly household income < €3000 <sup>a</sup>	0	–	–
	Monthly household income ≥ €3000	0.103	0.037	0.005*
Percentage of protection	Age	–0.007	0.004	0.045*
	No previous knowledge about disease <sup>a</sup>	0	–	–
	Previous knowledge about disease	0.173	0.082	0.034*
Probability of common adverse events	Monthly household income < €3000 <sup>a</sup>	0	–	–
	Monthly household income ≥ €3000	0.093	0.042	0.027*
Vaccine recommendation	Gender male <sup>a</sup>	0	–	–
	Gender female	0.217	0.078	0.005*

RI relative importance, SD standard deviation

<sup>a</sup>Reference value

\*Significant attribute level, *p*-value < 0.05

considered (age and time of professional experience).

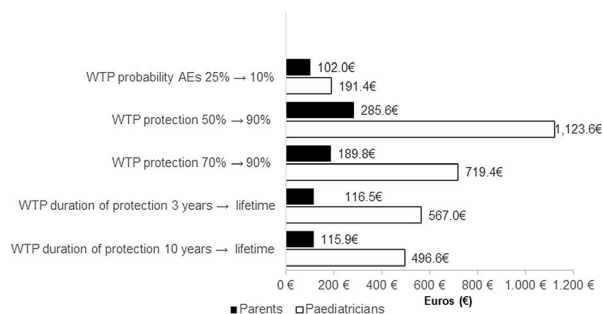
### WTP/Monetary Valuation of the Benefits Provided by the Vaccine

The WTP of parents was lower than that of pediatricians (considered in this latter group as the monetary valuation of the benefits provided by the vaccine) for all attribute levels evaluated (3 and 10 years of duration of protection, 50% and 70% of protection, 25% probability of AEs). Both groups were willing to pay/assign a higher

monetary valuation for a longer duration of protection, a lower probability of suffering AEs, and a higher percentage of protection, the latter being the attribute with the highest WTP/monetary valuation (Fig. 2).

### Sensitivity Analysis

Sensitivity analyses were conducted to identify whether (1) the proportion of surveyed parents with free access to MenB vaccine through their regional immunization program and (2) the type of practice of pediatricians (only private or



**Fig. 2** Parents’ and paediatricians’ WTP/monetary valuation of a clinical benefit. Willingness to pay (WTP)/monetary valuation for decreasing adverse events (AEs) from 50% to 10% not estimated, as 50% AEs level did not significantly affect preferences

public, as they could have different preferences about cost or other attributes) could affect the RI. In the subgroup of parents, participants from Castilla y León and Canary Islands, two autonomous regions where MenB vaccine was publicly funded at the time of study conduct ( $n = 19$  and  $n = 5$ , respectively; 8.6% of total parents), were eliminated from the analysis. For the subgroup of paediatricians, those working only in the private sector ( $n = 21$ ; 10.5% of total paediatricians) were eliminated from the analysis. The results of the sensitivity analysis showed no differences in terms of the RI given to the different attributes by parents or paediatricians, with respect to the full sample (Supplementary Table S4).

## DISCUSSION

There is currently growing interest in the use of choice-based experiments to elicit preferences for a variety of vaccines and to understand factors influencing vaccine decision-making of different groups of individuals [18]. The present study reported the results of a DCE about societal (parental and paediatrician) preferences for vaccination of children against MenB. Some previous DCE studies dealing with vaccines have been conducted worldwide, but only a few so far have focused on MenB [12]. To the best of our knowledge, this is the first such study to survey parents and paediatricians nationwide in Spain and explore preferences about MenB

vaccines (and possible heterogeneity of this preference).

We found that parents are more cost sensitive than paediatricians (the cost of the vaccine being their main driver for decision-making). Of note, MenB vaccines are not widely included in Spain’s NIP [28], being mainly available for private purchase. Therefore, the cost of the vaccine, when not publicly funded, could impose an access barrier, specifically for lower-income families. Indeed, parents with a low monthly household income ( $< €3000$ ) assigned higher RI to vaccine cost than those with a high income ( $\geq €3000$ ). In favor of this, a recent ecological study performed in Spain reported that access to the MenB vaccine was associated with the income level of families at the municipal level, producing inequities in the context of no national public funding [29]. In a 2013 survey of 523 family physicians in South Australia, the high cost of the MenB vaccine (non-publicly funded) and perceived low socioeconomic status of families were identified as barriers to vaccination, considered as “definitely a barrier” by 61% and 59% of respondents, respectively [30]. Of note, vaccination should not be in any case left to the economic capacity of citizens and should not generate inequities [31].

This role of cost in vaccination decision-making has mixed support in the literature. Cost has been identified in other studies as a strong attribute driving decision-making in relation to potential uptake of MenB vaccine, with most DCEs finding similar results for non-reimbursed or partially reimbursed vaccines in children [12, 16]. For example, a DCE study showed that when out-of-pocket costs of a vaccine increased from 0 to 100 euros, the uptake decreased by 10–13% from reference among Swedish, Dutch, Spanish, and Polish respondents [32]. In a qualitative study based on semi-structured interviews of parents, high cost was identified as a reason for low uptake of non-publicly funded vaccines [33]. A study on general practitioner recommendations for non-publicly funded vaccines showed variability in prescribing, with cost reported as the most frequent reason parents refused recommended (but non-publicly funded) vaccines for their

children [34]. However, some other studies found that the out-of-pocket cost of the vaccine was less important than other attributes, with parents attaching higher importance to prevention of severe diseases [19], or even with cost not being a factor leading to preference of a vaccine [35].

Accessibility (the lower the time and cost incurred by individuals to be vaccinated, the more accessible a vaccine will be), as well as effectiveness, disease burden, or vaccine-related side effects are important determinants of whether people become vaccinated [16]. Health policy institutions are instrumental in achieving and sustaining high vaccination coverage by making vaccines as accessible as possible. In Spain, several autonomous regions follow meningococcal vaccination calendars different from the official schedule. This situation further aggravates the inequity that already exists in terms of protection against meningococcal disease based on the public funding of the vaccines according to the region [36]. Therefore, introduction of a vaccine into the NIP and clear recommendations from health authorities are likely to increase vaccine uptake and promote equity [8, 34].

Despite the vaccination cost, most parents are eager to obtain the protection the vaccines can afford their children. In this regard, a doctor's recommendation to administer optional vaccines has proven to weigh heavily in parents' decision-making [33]. In the present study, recommendations of scientific societies and health authorities were highly valued by both parents and pediatricians. In another study, the advice of family and/or friends regarding vaccination and the advice of physicians strongly affected vaccine preferences in Sweden, in contrast to Poland and Spain, where the advice of (international) health authorities was more decisive [32].

Additionally, efficacy, especially in terms of degree of protection, was found to be relevant for both parents and pediatricians, as previously found for other pediatric vaccines [19, 37–39]. Duration of protection conferred by the vaccine was also considered important [12]. Both MenB vaccines currently available (4CMenB and MenB-fHbp) require two to three doses, with

the possibility of a booster vaccine. In this regard, the 12-month booster has been shown to protect against MenB disease for at least 2 years [40]. Moreover, it has been demonstrated that booster vaccination induced robust anamnestic responses, indicating effective priming by MenB vaccines across age groups [41].

It is reassuring, given that studies to date have shown variable waning of antibody levels in children following infant MenB vaccination [12]. This is particularly important because the highest burden of MenB occurs mainly during the first 3 years of life [42].

Therefore, efficacy (defined as percentage and duration of protection) and vaccine safety (prevention of potential side effects) are valued by both parents and pediatricians, being their monetary valuation of these attributes more favorable.

Our study indicated that both parents and pediatricians are more concerned about the effectiveness of a new vaccine than about potential side effects, at least for MenB vaccine. The same conclusion was found in a previous DCE regarding MenB [12]. Regarding other vaccines, previous literature has often identified side effects as a major concern for parents [19, 38], whether severe or common side effect (as in our study).

Regarding age at vaccination, both parents and pediatricians showed a greater preference for vaccination at any age (from 2 months) than for vaccination from the age of 10 years. In this regard, the 4CMenB vaccine can be administered from 2 months old, and the MenB-fHbp vaccine from 10 years and older. This aspect of vaccination at early ages seems to be specifically crucial for pediatricians, who assign a much higher RI than parents. In a previous study assessing pediatricians' preferences for specific features of hypothetical infant meningococcal vaccines, respondents also preferred protection at an earlier age. Nonetheless, the age at which protection begins was found to be less important than other attributes (such as vaccine effectiveness and number of injections) [43]. It has to be considered that this latter study included meningococcal vaccines in general, as



well as different age ranges (4 months, 12 months, 2 years) compared with our study.

Another interesting finding was the fact that parents with prior knowledge of the disease assigned a higher RI than those without to the percentage of protection. Perception of the severity of the disease could be a main driver to accept the use of a new vaccine, so public information for increasing disease awareness may play a role in increased vaccine acceptance by the general population.

### Study Limitations

Despite DCE being the recommended approach to assess preferences, there is always a risk of a gap in how preferences are grasped; the study participants might make other choices in real life [13, 44]. It is important to highlight that respondents' preferences and choices were constrained within the attributes and levels presented in the discrete choice sets; so societal preferences for vaccination may include attributes not explored in the present study. Nonetheless, the attributes and levels tested herein were selected according to the literature and the input of a scientific committee of experts.

Sample size calculations are particularly difficult for DCE applications in healthcare [13]. Most published studies have a sample size of 100–300 respondents [45]. Orme recommends sample sizes of at least 300, with a minimum of 200 respondents per group for subgroup analysis [22]. As no previous information from similar studies was available for estimating this sample size, the DCE was conducted with a convenience sample of a minimum of 200 individuals for each group (parents and pediatricians). In this regard, the sample of the study is aligned with Orme's general recommendation to reflect the preferences of the targeted society for a given treatment. Given that the study population is limited to Spain, results should be interpreted within the context of the study. Extrapolations to other situations should be approached with caution.

Finally, regarding the measure of cost (WTP/monetary valuation), one limitation of

the present study could be that an altruistic interpretation of cost was used for pediatricians, which is in contrast to the assumptions for parents (i.e., the interpretation of cost differs).

## CONCLUSION

Recommendations of scientific societies and healthcare authorities and percentage of conferred protection appear to be key factors in the decision of parents and pediatricians to vaccinate children against MenB. The fact that cost appears to bear more importance to parents than pediatricians could at least partly reflect that, for the latter, a more altruistic approach to vaccination is followed. To pediatricians, age at vaccination appears relatively more important in the present study. Altogether, these findings could be useful for decision-making regarding MenB vaccination of children in settings where no funding program exists. The present study lends further support to the importance of considering societal preferences for MenB vaccine inclusion in the NIP.

## ACKNOWLEDGMENTS

**Trademarks.** Bexsero is a trademark owned by or licensed to GSK. Trumenba is a trademark of Pfizer.

**Funding.** GlaxoSmithKline Biologicals SA funded this study (study number: VEO-000341) and was involved in all stages of study conduct, including analysis of the data. GlaxoSmithKline Biologicals SA proposed the steering committee members; however, the funder was not involved in their activities or decisions. GlaxoSmithKline Biologicals SA also took in charge all costs associated with the development and publication of this manuscript, including the journal's Rapid Service Fees.

**Medical Writing, Editorial, and Other Assistance.** The authors thank Outcomes'10 for writing support and Business & Decision Life

Sciences platform for editorial assistance and manuscript coordination, on behalf of GSK.

**Authorship.** All named authors meet the International Committee of Medical Journal Editors criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

**Author Contributions.** All authors contributed to the study conception and design. Data collection and analysis were performed by Clara Gabás-Rivera, Marta Comellas, and Miriam Prades. All authors critically reviewed the results of the study. All authors revised and commented on this version of the manuscript. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

**Disclosures.** Federico Martín-Torres has received honoraria from GSK, Pfizer Inc, Sanofi Pasteur, MSD, Seqirus, Biofabri and Janssen for taking part in advisory boards and expert meetings and for acting as a speaker in congresses outside the scope of the submitted work. Federico Martín-Torres has also acted as principal investigator in randomized controlled trials of the above-mentioned companies as well as Ablynx, Gilead, Regeneron, Roche, Abbott, Novavax, and MedImmune, with honoraria paid to his institution. Ángel Gil de Miguel and Jesús Ruiz-Contreras have received consulting fees from GSK. Laura Amanda Vallejo-Aparicio, Andrea García, María del Carmen González-Inchausti, Eduardo de Gomensoro, and Zeki Kocaata are employed by GSK. Laura Amanda Vallejo-Aparicio and Eduardo de Gomensoro also hold shares in GSK. Clara Gabás-Rivera, Marta Comellas, Miriam Prades, and Luis Lizán are employees of Outcomes'10, and Outcomes'10 received funding from GSK for carrying out the study. Authors declare no other financial and non-financial relationships and activities.

**Compliance with Ethics Guidelines.** The study was evaluated by the Ethics Committee of the Hospital Universitario Puerta de Hierro,

which considered that the study did not require an opinion or follow-up by the Ethics Committee as a biomedical research project and that there was no ethical or legal impediment to its realization. Parents and pediatricians voluntarily accepted to participate in the study. The study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. No economic compensation was offered to participants.

**Data Availability.** Information on GSK's data sharing commitments and requesting access to anonymized individual participant data and associated documents can be found at [www.clinicalstudydatarequest.com](http://www.clinicalstudydatarequest.com).

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