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Cost of illness of invasive meningococcal disease caused by serogroup B *Neisseria meningitidis* in Spain

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ABSTRACT

Introduction: Invasive meningococcal disease (IMD) is a severe infectious disease, mainly affecting children under 5 years, associated with long-term physical, neurological and psychological sequelae. In Spain, most IMD cases are caused by meningococcal serogroup B (MenB). This study estimates its economic burden from a societal perspective in Spain.

Methods: A previously published bottom-up, model-based incidence costing approach by Scholz et al. (2019) to estimate the economic burden of MenB in Germany was adapted to the Spanish setting. Diagnosis and age-related costs for a hypothetical Spanish cohort were calculated over a lifetime horizon. Official Spanish databases, literature and expert opinion were used as data sources. The costs were updated to 2019 prices, and a 3% discount rate was applied. Direct costs related to the acute IMD phase, long-term sequelae, rehabilitation and public health response were considered. Indirect costs included productivity losses and premature mortality and were calculated using the human-capital approach (HCA) and friction-cost approach (FCA). Deterministic and probabilistic sensitivity analyses were also performed.

Result: At base-case, the total cost for a cohort of 142 patients (2017–2018 period) was €4.74 million (€33,484/case) using the FCA and €13.14 million (€92,768/case) using the HCA. Direct costs amounted to €4.65 million (€32,765/case). Sequelae costs represented 62.46% of the total cost using the FCA and 77.63% using the HCA. Deterministic sensitivity analysis showed that variation of ± 20% in the input parameter values (population, epidemiology, productivity, costs) had the greatest influence on the base-case results, and the probabilistic sensitivity analysis showed the probability of fitting base-case estimates was > 99%, both for FCA and HCA.

Discussion: MenB IMD is an uncommon but severe disease, with a high economic burden for Spanish society. The elevated costs per IMD case reflect its severity in each patient suffering this disease, especially due to the development of sequelae.

1. Introduction

Invasive meningococcal disease (IMD) is a severe and life-threatening infectious disease, associated with high mortality rates of 10% and more, even with the use of aggressive treatment [1]. IMD is caused by the bacterium *Neisseria meningitidis*, which is commonly present asymptomatically in the nasopharynx of adults but can cause meningitis or septicaemia if it becomes invasive [2,3]. The highest incidence of IMD occurs among infants and young children aged less than 5 years; it is associated with long-

Abbreviations: ADHD, attention deficit hyperactivity disorder; COVID-19, coronavirus disease 2019; FCA, friction cost approach; HCA, human capital approach; IBECS, Índice Bibliográfico Español en Ciencias de la Salud; IMD, invasive meningococcal disease; INE, National Institute of Statistics (*Instituto Nacional de Estadística*); IQ, intelligence quotient; MEDES, medicine in Spanish (*MEDicina en ESpañol*); MenACWY, meningococcal serogroups A, C, W and Y; MenB, meningococcal serogroup B; MenC, meningococcal serogroup C; OBAC, Official Bulletins of Autonomous Communities; RENAVE, National Epidemiological Surveillance Network (*REd NAcional de Vigilancia Epidemiológica*).

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term physical, neurological and psychological sequelae including hearing loss, mental retardation, complications that can require limb amputation, seizures, cognitive deficits, difficulties with learning and memory skills, and anxiety [1,4].

In Spain, IMD cases are reported weekly through the National Epidemiological Surveillance Network (RENAVE; REd NAcional de Vigilancia Epidemiológica). This database includes clinicians' reports of culture-proven cases that classify IMD cases by their specific serogroup. IMD incidence has decreased notably in recent years, from 1,625 cases (4.04 cases per 100,000 population) in 1999–2000 to 346 cases (0.74 cases per 100,000 population) in 2017–2018 [5]. As in the rest of Europe, meningococcal serogroup B (MenB) is responsible for most of the IMD cases in Spain, accounting for 41% of total IMD cases in 2017–2018 (i.e.,142 cases, 0.30 cases per 100,000 population). Its incidence is highly age-dependent, being most frequent in infants aged less than 1 year (5.85 cases per 100,000 population), followed by children aged 1–4 years (1.80 cases per 100,000 population). However, mortality rates of IMD caused by MenB are higher in adolescents (aged 10–14 years: 25.00%) and older adults (aged $\geq$ 65 years: 19.35%) [5] (see **Annex I, Table 1**).

The current National Immunisation Programme for IMD in Spain includes vaccination against serogroups A/C/W/Y, with a dose against meningococcal serogroup C (MenC) in infants aged 4 months and a dose against meningococcal serogroups A, C, W and Y (MenACWY) at 12 years of age [6]. MenB vaccine is only recommended in situations of special risk of acquiring IMD disease and in case of outbreaks [7]. However, since 2019, some Spanish regions (i.e., Castilla and Leon and the Canary Islands) include the MenB vaccine as part of their regional immunisation programmes, meaning that the vaccine is free of charge for families [8,9].

As shown in previous studies [10,11], IMD is associated with a considerable economic burden from a healthcare payer perspective, in particular due to its rapid onset and the significant risk of long-term disability, involving longer inpatient stays and higher hospitalisation costs. In Spain, three large studies have been conducted that tried to estimate this burden: the first two studies evaluated the burden of hospitalisations due to IMD, regardless of serogroup, from 1997 to 2008 [3] and from 1997 to 2005 [12]; the third study explored the lifelong rehabilitation costs associated with treating two survivors of severe IMD who experienced long-term sequelae [13]. To date, no study has analysed the full economic burden of MenB IMD in Spain, including the indirect costs associated with MenB and the management of its long-term sequelae. The aim of this study, therefore, was to estimate the economic burden of MenB IMD in Spain from a societal perspective.

2. Methods

A model, previously developed and used to estimate the economic burden of MenB IMD in Germany in 2019 [11], was adapted to the Spanish setting by making some relevant modifications, as described in this section. The most recent data available at the time the study was conducted were used for the analysis.

2.1. Study design and population

Following Scholz et al.'s methodology [11], a bottom-up, model-based incidence and costing study design approach was used [14], calculating costs over a lifetime horizon, with a discount rate of 3% (0% and 5% for the sensitivity analysis) applied to costs and health outcomes, as is recommended for Spain [15].

Population data by sex and age (0–100 years) for 2019 were obtained from the National Institute of Statistics (INE, *Instituto Nacional de Estadística*) [16]. Life expectancy according to sex and age was estimated based on 2018 records obtained from the INE [17]. MenB IMD data (both incidence and mortality rate) were extracted from the 2017–2018 RENAVE report, which did not make a distinction between male or female data [5]. Cases were reported on a weekly basis by culture-proven serogroup. IMD cases, where no confirmation on the serogroup was proven or was not possible to establish, were reported as "non-classifiable". The current study includes only those classified as MenB IMD [5]. The number of MenB IMD cases was expressed as incidence per 100,000 population. The mortality rate was calculated as the number of deaths divided by the total number of MenB IMD cases (see **Annex I, Table 1**).

2.2. Data sources

Data relating to epidemiology, survival rates, health care resources, special education needs, formal and informal care and productivity losses were obtained from the following databases: GuíaSalud (library of Clinical Practice Guides of the Spanish National Health System); IBECS (Índice Bibliográfico Español en Ciencias de la Salud); MEDES (MEDicina en Español); PubMed; Google Scholar; Official Bulletins of Autonomous Communities (OBAC); Bot PLUS; INE; the Statistics Website of the Ministry of Health; Consumer Affairs and Social Welfare (*Portal Estadístico del Ministerio de Sanidad, Consumo y Bienestar Social*); and RENAVE.

The search was conducted in English and Spanish and focused on observational studies, systematic literature reviews and *meta*-analyses. The keywords included: 'serogroup B meningococcal disease'; 'Meningococcal serogroup B'; '*Neisseria meningitidis* group B'; 'Meningococo serogrupo B'; 'enfermedad meningocócica del serogrupo B'; '*Neisseria meningitidis*'; 'MenB'; and 'Meningitis B'. Additional terms were added according to specific conditions (e.g., hearing loss and renal disease).

2.3. Total costs

All direct and indirect costs associated with the management of MenB IMD were considered (see Fig. 1) and updated to 2019 prices based on the Health Consumer Price Index [18] at the point at which the analysis was carried out.

Direct cost data were drawn from the OBAC and included: treatment for acute IMD, public health responses (prophylactic treatment given to contacts of MenB IMD cases), professional care, other subsidies for long-term sequelae, rehabilitation and special education needs (see **Annex I, Table 2**). Due to the high variability of the data, median costs were used for the analysis. Indirect costs included: productivity losses (for patients or parents) and premature mortality due to MenB IMD; these were calculated using the friction cost approach (FCA) and the human capital approach (HCA) [19–21]. The FCA is a conservative approach where only the costs incurred by employers in replacing a sick worker, the so-called friction period, are taken into account to calculate indirect costs (employer perspective). The HCA considers all productivity losses, including the friction period losses, to estimate indirect costs (employee perspective) [19–21].

2.3.1. Direct costs related to the acute phase of IMD

Costs associated with hospitalisation, post-exposure prophylaxis as a public health response and neurological rehabilitation were included in this category. Hospitalisation costs by age were published by the Spanish Ministry of Health [22] (see **Annex I, Table 3**). Prophylactic treatment costs for MenB IMD contacts were estimated at €816.69 per MenB IMD patient, taking into account: (i) the retail price of the three commercialised rifampicin formulations in Spain [23]; (ii) the distribution by age and average weight

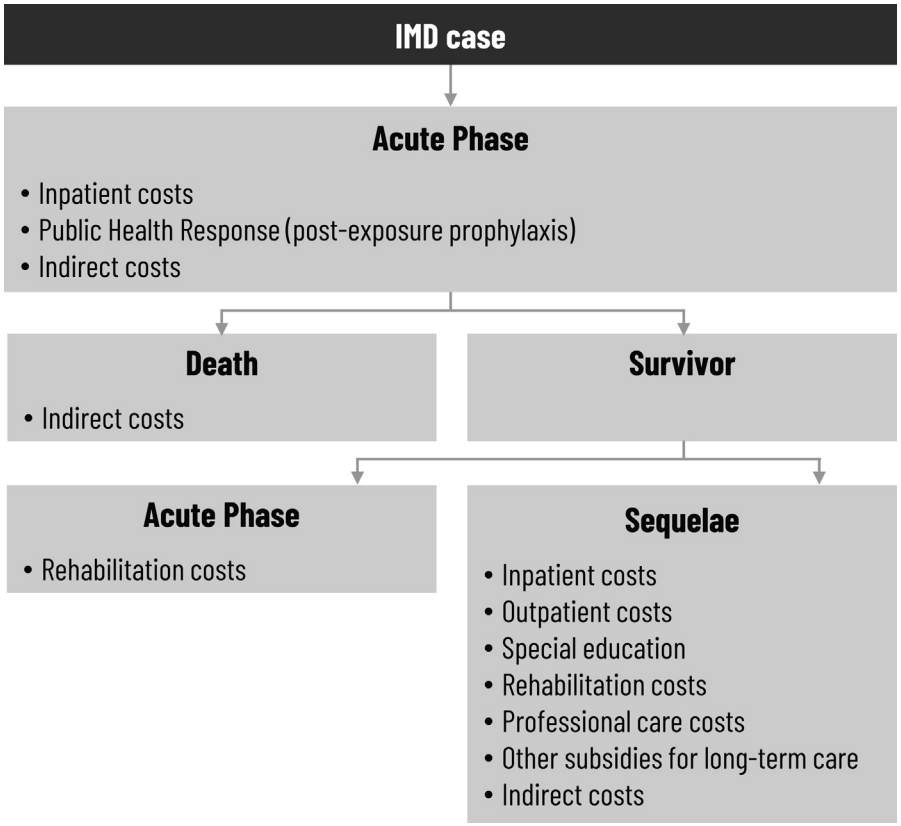

Fig. 1. Schematic flow chart of the cost calculation for a case of invasive meningococcal disease (IMD).

of contacts [24]; (iii) the average number of contacts per MenB IMD case (10.92 contacts, based on the German model) [25]; and (iv) the number of visits to a general practitioner to receive treatment (detailed in **Annex I, Tables 4, 5 and 6**). Neurological rehabilitation costs (i.e., cost per session needed, including both short- and long-term rehabilitation) by age were calculated, taking into account the probability of requiring rehabilitation, the number of sessions and the unit cost per session (see **Annex I, Table 3**). The probability of requiring rehabilitation and the number of sessions attended were obtained from Scholz et al.'s study [11], due to a lack of equivalent data in Spain. The unit cost refers to the mean cost of one neurological rehabilitation session, obtained from the OBAC (€105.79).

2.3.2. Direct costs related to IMD sequelae

The probabilities of experiencing sequelae related to IMD were extracted from the previous German study (see **Annex I, Table 7**). Direct costs were estimated for inpatient and outpatient care, lifelong rehabilitation, special education needs and professional care and subsidies.

Direct costs for inpatient and outpatient care were adapted to the Spanish setting, using data from the Spanish Ministry of Health database and the OBAC. Data were extracted separately for costs during the first year and for the second year and beyond (see **Annex I, Table 7**).

Direct costs for lifelong rehabilitation were calculated based on Darbà et al. study and assumed that just 5% of patients with long-term sequelae (i.e., cochlear implant, neurological disability, limb amputation and renal disease) would receive lifelong therapy [13]. This assumption of using just 5% of the total cost estimation was made on the basis that Darbà and colleagues only analysed the cost relating to two very severe cases of IMD, although a sensitivity analysis for 100% was included to show the variation in base-case results. The median direct cost for lifelong rehabilitation amounted to €860.83 per year.

Direct costs for special education needs (i.e., children aged 1 to 15 years who survived MenB IMD and suffered mental retardation and learning disabilities [2]) were calculated according to the type of sequelae and included costs for educational assistance, attendance at a special school and transport to and from school (see **Annex I, Table 8**) [13]. Professional care and subsidies were also included as direct costs, where these data were available in Spain for people with disabilities [26]. The distribution by type of disability (physical and others, sensory, intellectual, and mental) was extracted from the INE (2018) and used to estimate professional and subsidies costs, which were then assigned to each type of sequelae (see **Annex I, Table 8**) [27].

2.3.3. Indirect costs

Indirect costs were calculated separately based on: (i) productivity losses due to the acute phase of IMD; (ii) premature mortality; and (iii) reduced productivity due to long-term sequelae.

Indirect costs for productivity losses due to the acute phase of IMD were calculated with an adjusted friction period (i.e., the time required to replace a worker in Spain) of 75 days (75 or 105 for the sensitivity analysis) [19]. The percentage of the general working population and the average yearly income by age and sex were retrieved from the INE [28,29] (see **Annex I, Table 9**). For children aged less than 18 years, one parent (zero or two parents for the sensitivity analysis) was assumed to be absent from work during the child's hospitalisation. The average age of a mother in Spain at the birth of their first child was 32 years in 2019 [30]. As reported in the German study, there was no difference when using the HCA or the FCA, as all of the average length-of-stay estimates of the acute phase of IMD were less than the friction period of 75 days [11].

Indirect costs related to premature mortality were calculated using the friction period, income [29], and life expectancy at the time of death (Spanish life expectancy table for 2018 [17]). Patients aged less than 15 years resulted in no indirect costs under the FCA as they do not belong to the labour force.

The indirect costs of reduced productivity due to long-term sequelae were calculated based on the annual salary of the disabled population stratified by type of disability (physical and others, intellectual, mental or sensory) in 2018 [31]. The productivity of employed individuals with disabilities was estimated by dividing the annual salary of the disabled population stratified by type of disability by the annual salary of individuals without disabilities (€24,009.12 in 2018 [29]). The unemployment rate due to disability stratified by type of disability was calculated by dividing the employment rate of the disabled population stratified by type of disability [32] by the employment rate of the non-disabled population (50.05% in 2018) [29]. Unemployment due to disability was calculated using the difference (1 – the proportion of employment rate with disability/employment rate without disability). The average productivity for the disabled population was calculated using the average productivity of unemployed (0% productivity) and employed (54.82% for physical; 19.44% intellectual; 24.03% mental; and 76.36% sensory) disabled people. Finally, the productivity percentages were assigned to each type of sequela: 76.36% (23.64% loss of productivity) with hearing loss and blindness; 19.44% (80.56% loss) with severe neurological disability, mental retardation and speech problems; 54.82% (45.18% loss) with motor deficits, limb amputation, epilepsies/seizures, skin scarring or renal disease; and 24.03% (75.97% loss) with psychological impairments (detailed in **Annex I, Tables 10 and 11**).

2.4. Sensitivity analysis

Two types of sensitivity analysis were carried out to demonstrate the robustness of the base-case results: deterministic sensitivity analysis and probabilistic sensitivity analysis.

The variables for the deterministic sensitivity analysis included: discount rate and population (in terms of age, sex and life expectancy); MenB IMD cases and deaths; friction period; whether parents were absent from work; elasticity productivity; average yearly income and workforce participation rate; direct and indirect costs due to the acute phase of IMD and sequelae; percentage of patients that received lifelong rehabilitation therapy; and the probabilities of experiencing sequelae (detailed in Table 1**)** [2,15,22].

For the probabilistic sensitivity analysis, the variables included: 1,000 simulations in which the study parameters were simultaneously varied (i.e., population, life expectancy, incidence of MenB IMD, mortality due to MenB IMD, probability of sequelae, workforce participation rate, salary, costs and rates/probabilities) according to different distributions (detailed in **Annex I, Table 12)**.

3. Results

3.1. Total disease burden

At base-case, the total cost associated with MenB IMD from a societal perspective for a hypothetical cohort of 142 patients (cases reported in 2017–2018) (detailed in **Annex I, Table 1**) was €4.74 million measured with the FCA and €13.14 million measured with the HCA (Table 2), which corresponds to €33,484 and €92,768 per case, respectively. Sequelae cost represented 62.46% and 77.63% of the total cost using the FCA and the HCA, respectively, with total direct costs amounting to €4.6 million in both estimations. Indirect costs calculated by the HCA were higher, mainly due to the estimates for premature mortality (detailed in Table 2).

Table 1
Additional values and probabilities in the deterministic sensitivity analysis.

	Base-case	Alternative scenario
Additional values		
Discount rate	3%	0%; 5%
Friction period	75 days	75 days; 105 days
Parents absent from work[a]	1	0; 2
Elasticity productivity	1	0.8; 1
Patients that received lifelong rehabilitation therapy	5%	100%
Low/high parameter values [b]	–	–20%; +20%
Additional probabilities for sequelae		
Hearing loss:		
Cochlear implant	2.45%	0.56%
Moderate bilateral	3.80%	0.87%
Moderate unilateral	5.21%	1.19%
Neurological disability:		
Severe neurological	1.02%	0.77%
Mental retardation	0.50%	0.38%
Speech problems	3.56%	2.70%
Motor deficits	1.53%	1.16%
Limb amputation	**1.26%**	2.18%
Epilepsy/seizures	**1.78%**	1.78%
Skin scarring	**6.39%**	2.62%
Renal disease	**2.05%**	1.75%
Blindness	**0.42%**	0.42%
Psychological impairments:		
ADHD	9.66%	9.66%
Anxiety	2.25%	2.25%
Separation anxiety	5.96%	5.96%

Abbreviation: ADHD, attention deficit hyperactivity disorder.
[a] 0 = assuming a grandparent takes care of the child; 2 = assuming both parents are absent from work.
[b] Parameter values take into account: population, epidemiology and productivity data; direct and indirect costs of the acute phase of invasive meningococcal disease; probability of sequelae and of requiring long-term informal care; and direct and indirect costs due to sequelae.

Table 2
Economic burden of meningococcal serogroup B invasive meningococcal disease (IMD).

		FCA [21]	HCA [33]
Acute IMD phase			
Direct costs		€1,735,718	
Indirect costs	Acute IMD phase	€42,426	
	Premature deaths	€1,791	€1,160,527
Sequelae			
Direct costs		€2,916,955	
Indirect costs		€44,194	€7,279,633
Total		**€4,741,085**	**€13,135,260**
Per case[a]		**€33,484**	**€92,768**

Abbreviations: FCA, friction cost approach; HCA, human capital approach.
[a] Total cost/142 cases.

3.2. Burden of the acute IMD phase

The direct costs of the acute IMD phase amounted to almost €1.74 million or €12,223.36 per case (Table 2). As shown in Fig. 2, the greatest direct costs were observed for children with the highest IMD incidence, in the 1 to 4 years age group (€311,561) (31 cases, 1.80 cases per 100,000 population; **Annex I, Table 1**), comprising 18% of the total direct costs, followed by newborn babies (aged less than 1 year, €264,217) (23 cases, 5.85 cases per 100,000 population; **Annex I, Table 1**) (detailed in **Annex I, Table 13**).

For indirect costs, irrespective of the approach taken, given the duration of the acute IMD phase and the friction period, costs of €42,426 (€298.77 per case) were incurred due to productivity

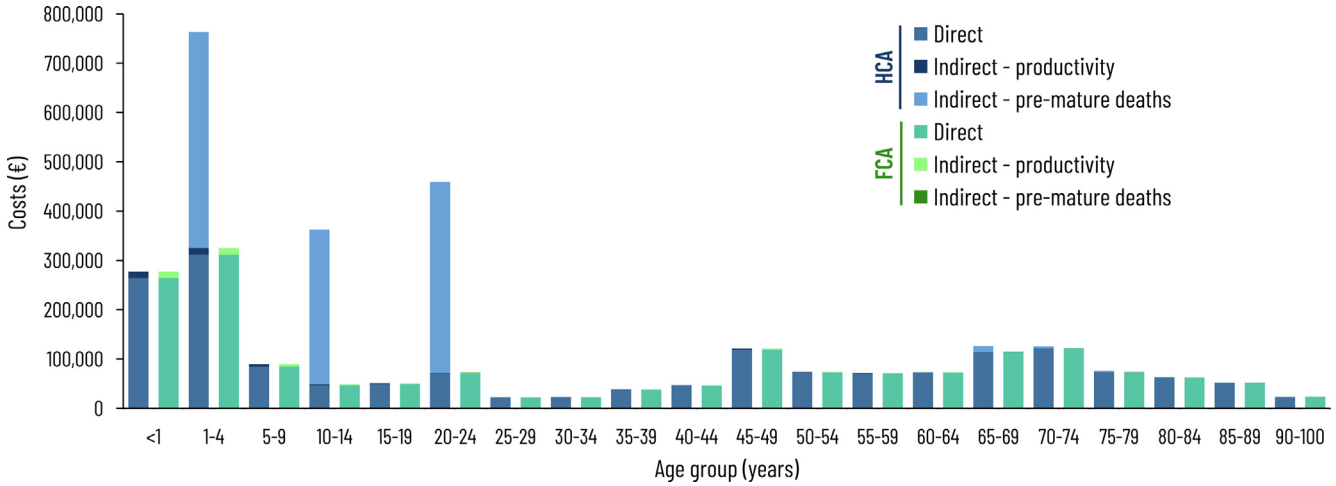

Fig. 2. Direct and indirect costs of the acute phase of invasive meningococcal disease per age group. Abbreviations: FCA, friction cost approach; HCA, human capital approach.

losses, of which 18.1% (€7,685) corresponded to patients and 81.9% (€34,742) to parents (Fig. 2, Table 2**, and Annex I, Table 13**). Using the HCA, premature deaths had a huge impact, especially among individuals aged 1–4 years (€737,738), 10–14 years (€328,981) and 20–24 years (€387,313) (**Annex I, Table 14**).

3.3. Burden of long-term sequelae

The total cost associated with each type of sequela is defined by the probability of the specific sequelae and the costs per type of sequelae (see **Annex I, Table 15**).

As shown in Table 2, the total direct costs associated with sequelae amounted to €2.92 million (€20,601 per case). Total indirect costs were estimated at €44,194 for the cohort (€312 per case) when using the FCA and €7.3 million (€51,413 per case) when using the HCA.

Fig. 3 shows the percentages of direct cost generated by sequelae type. The costliest sequelae in most age groups were psychological impairment (mostly due to attention deficit hyperactivity disorder [ADHD]), followed by renal disease, hearing loss and neurological disability. The percentage of direct costs caused by neurological disability increments with age, being the costliest within the older age groups (detailed in **Annex I, Table 16**).

As shown in Fig. 4, ADHD is the costliest sequela, representing 26.6% and 25.1% of the total cost of sequelae when using the HCA and FCA, respectively, and with a direct cost of €732,045. ADHD results in a total cost (direct costs and patients' and parents' indirect costs) of €2.71 million (€197,707 per IMD case with ADHD), of which €732,045 is attributable to direct costs, €1.85 million to patients' indirect costs and €127,855 to parent's indirect costs when using the HCA. Using the FCA, it represents €743,591 (€54,208 per IMD case with ADHD), with €732,045 for direct costs, €9,541 for patients' indirect costs and €2,005 for parents' indirect costs. When estimated with the HCA, the indirect costs of ADHD amount to €1.98 million, while using the FCA, the indirect costs amount to €11,546. These elevated costs result from the higher incidence of this sequela. Separation anxiety is the second most expensive sequela according to the HCA, with a total cost of €1.29 million (€9,068 per case), followed by speech problems (€951.671, €6,702 per case), skin scarring (€870,580, €6,130 per case) and renal disease (€750,900, €5,288 per case). Using the FCA, the second costliest sequela is renal disease (€491,800, €3,463 per case), followed by epilepsy/seizures (€331,837, €2,337 per case) and cochlear implants (€229,029, €1,613 per case) (detailed in **Annex I, Table 7 and Table 15**).

3.4. Sensitivity analysis

Fig. 5 summarises the results of the deterministic sensitivity analysis using both FCA and HCA, with the bars on the left-hand

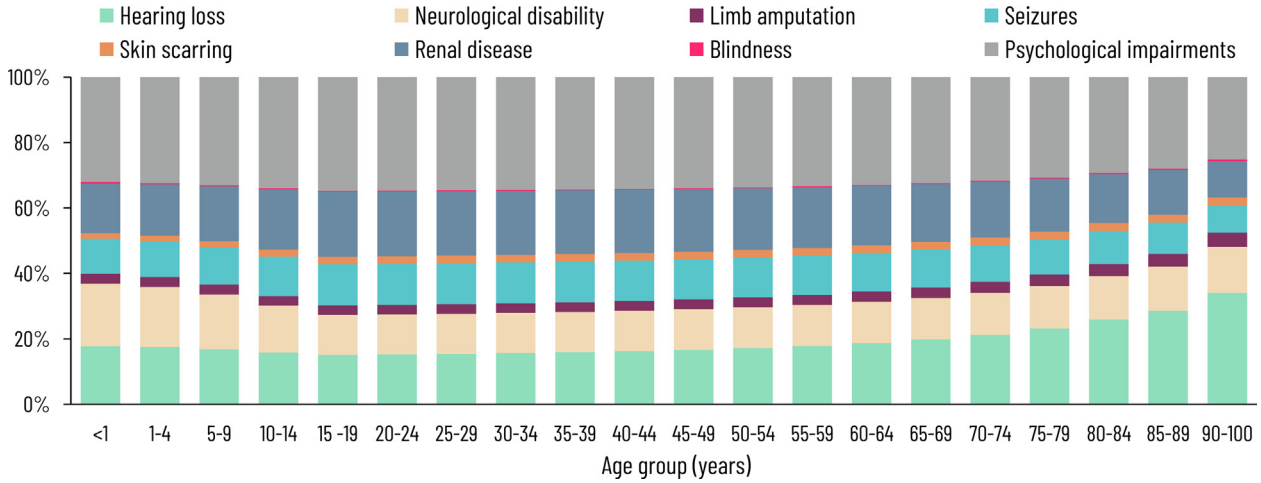

Fig. 3. Percentage of direct cost per average invasive meningococcal disease survivor per sequelae.

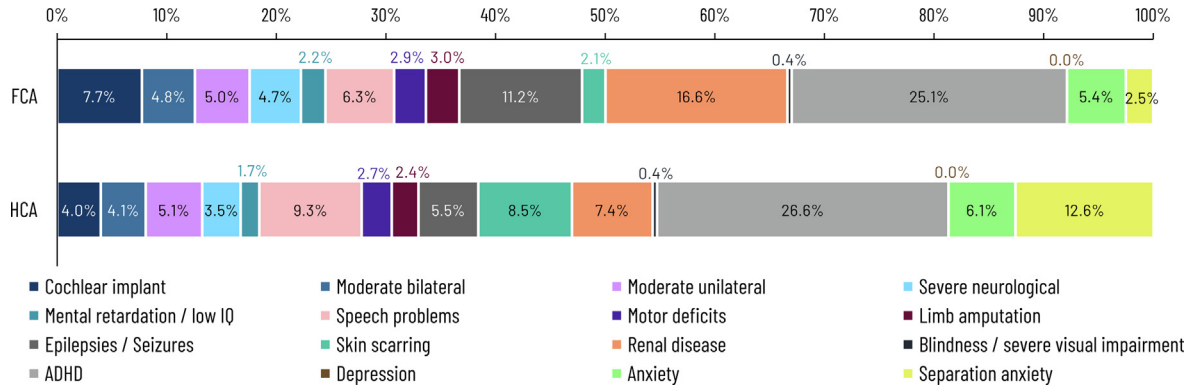

Fig. 4. Percentage of direct costs generated by sequelae type using HCA and FCA. Abbreviations: ADHD, attention deficit hyperactivity disorder; FCA, friction cost approach; HCA, human capital approach; IQ, intelligence quotient.

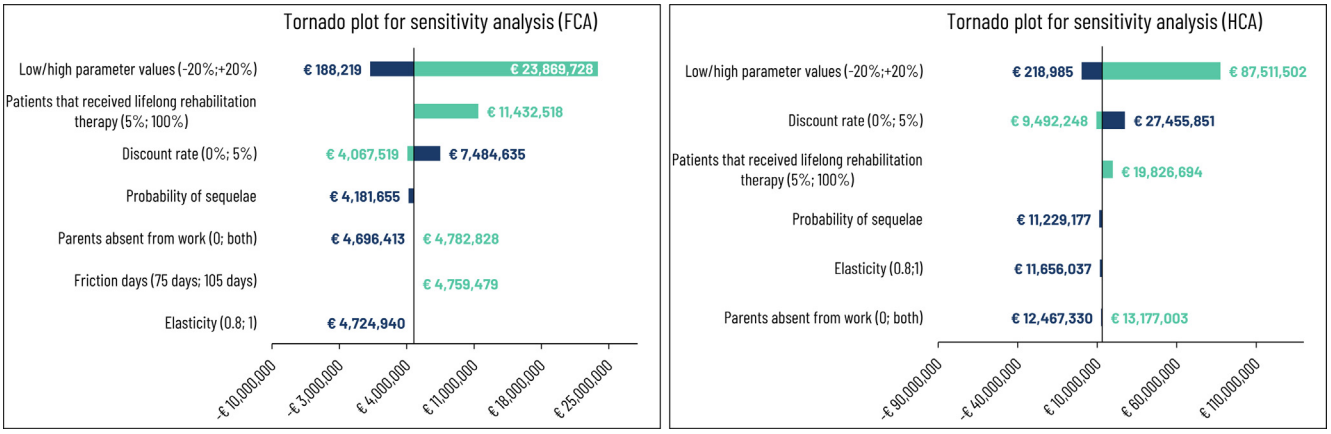

Fig. 5. Tornado plot showing the deterministic sensitivity analysis: FCA (left) and HCA (right). Abbreviations: FCA, friction cost approach; HCA, human capital approach.

side representing low parameter values and the bars on the right-hand representing high parameter values. The parameters with the greatest influence on the base-case results, for both FCA and HCA, were variation of ± 20% in the input values for the main parameter values (i.e., population, MenB IMD cases, MenB IMD deaths, probability of developing sequelae and requiring long-term informal care, direct and indirect costs of the acute IMD phase, direct and indirect costs due to sequelae, and other productivity parameters), followed by the percentage of patients that received lifelong rehabilitation therapy for the FCA and the discount rate for the HCA. As the friction period is less than 1 year, indirect costs calculated via the FCA were not affected by the discount rate as much as the indirect costs calculated by the HCA method were.

Fig. 6 shows the results of the probabilistic sensitivity analysis for the total population, considering the FCA and HCA, where the total mean costs are represented by dots. In this analysis, the probability of the total costs for both HCA and FCA fitting the point estimates (base-case generated) was > 99%.

4. Discussion

The economic burden of MenB IMD is highly age-dependent, with higher costs incurred at a younger age (i.e., from 0 to 4 years). This can be explained by the higher incidence of the disease among young children, the long-term sequelae associated with cumulative costs over a prolonged period, and the productivity loss for

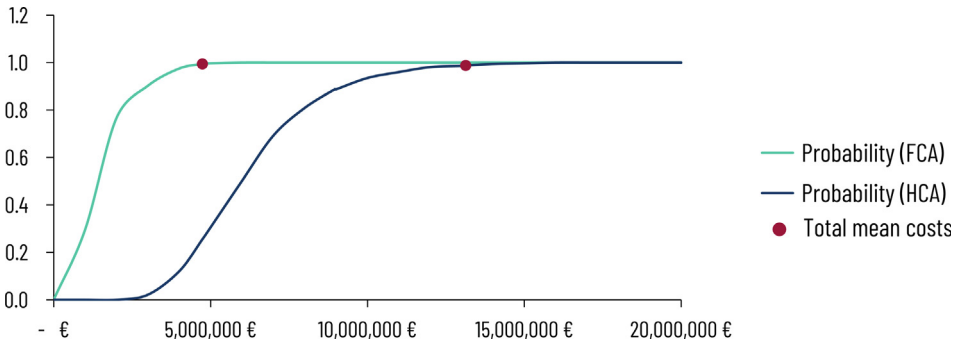

Fig. 6. Probabilistic sensitivity analysis for both the FCA and HCA methods. Abbreviations: FCA, friction cost approach; HCA, human capital approach.

patients and parents. The results also showed that the method used to estimate indirect costs (FCA and HCA) can have a large impact on estimates of the burden of the disease.

This is the first study to report on the burden of MenB IMD in Spain from a societal perspective; therefore, a comparison with previous results was not possible. At an international level, a similar study carried out in Germany by Scholz et al. in 2019 [11] estimated the burden of MenB IMD for a cohort of 343 patients to be €19.6 million using the FCA and €58.8 million using the HCA. These earlier results contrast with the total costs reported here for a cohort of 142 patients: €4.74 million (€33,484 per patient) using the FCA and €13.14 million (€92,768 per patient) using the HCA. However, some relevant differences in the study designs must be considered before comparing these results: first, the higher number of MenB IMD cases in the hypothetical cohort has a direct impact on the total economic burden calculations (343 versus 142); the friction period in the German study was set at 92 days while for the Spanish study the value used was 75; the ratio of men staying at home versus women staying at home was 0.5 in Germany and 0.76 in Spain; Spanish life expectancy was slightly longer but wages and the employment rate were lower than those in Germany [11,33].

Although comparisons with other studies on the burden of MenB IMD in Spain cannot be performed, a comparison with the economic burden of other infectious diseases in Spain can be conducted. Influenza epidemics in Spain have an average cost of €542.2 per case, as reported by Badia Llach et al., who investigated 662 cases [34]. Varicella infections cost €96.3 per case within a primary care setting in which 683 cases were evaluated [35]. Rotavirus-related acute gastroenteritis costs €166 per patient for primary care and €1,000 to €1,700 for hospitalisation [36]. These diseases have a greater incidence than MenB IMD but lower costs per case, which reflects the elevated clinical and economic impact of MenB-related IMD in both patients and caregivers.

Currently, MenB vaccination is not included as part of the National Immunisation Program in Spain, meaning that it can only be acquired privately [6]. However, in two regions (i.e., Castilla and Leon and the Canary Islands), MenB vaccine has been publicly funded since 2019 [8,9]. A recent study evaluated whether a possible statistic correlation could exist between the income per capita level of families and the MenB vaccination uptake in Spain in absence of national funding. A statistically significant correlation between these two variables at municipalities level was found, suggesting that differences in the income per capita level within the Spanish families could raise an inequity in the access to the vaccine [37].

The data used in this study were from 2017 to 2018, as these were the most recent data available at the time the study was performed. The updated data available for 2019–2020 showed a notable decrease in MenB IMD cases [38,39], with just 91 infections or 0.19 cases per 100,000 population, which represents a 73.70% reduction in the number of infections compared with the previous two-year period (346 infections, 0.74 cases per 100,000 population in 2017–2018) [5]. This is likely to have resulted from the social distancing and additional hygiene measures implemented since the beginning of the coronavirus disease 2019 (COVID-19) pandemic in March 2020, which had the side-effect of preventing the transmission of MenB IMD. Given that the 2020 data include the period of the COVID-19 pandemic, therefore, they would not be representative of the actual transmission situation, so the 2017–2018 data were used to enable a more accurate analysis. Our study had several limitations. First, as the number of cases was limited, the results were obtained by using an adapted economic model instead of real-world data, which would have allowed a better estimation of the impact of long-term sequelae of IMD. Such limitations are inherent to the use of economic models (i.e., assumptions are made to obtain results), so both deterministic and probabilistic sensitivity analyses were performed to mitigate this uncertainty. Second, long-term sequelae probability data were retrieved from a systematic literature review conducted by Olbrich et al. [4]. Local data from Spain were included in the deterministic sensitivity analysis that demonstrated a low impact on the base-case results compared with other input variations. Third, health-care cost data showed high variability among the autonomous communities of Spain; therefore, the median value was used for the analysis as being representative of the Spanish unit costs within the national health system. Fourth, there were no data on the cost of neurological rehabilitation for IMD cases in Spain, so the probability of requiring rehabilitation and the number of sessions attended were assumed, based on Scholz et al. [11] and applying Spanish costs. The same study was used to estimate the prospective population to be offered prophylactic treatment (i.e., 10.92 contacts/MenB IMD case). A similar calculation was made for Spain using data from the INE [40] and the Ministry of Education [41], but we decided to use the published data for this study. Finally, based on expert opinion and a previous publication by Darbà et al. [13], we assumed that just 5% of patients with extremely severe long-term sequelae would receive lifelong rehabilitation therapy. The impact of this assumption was analysed by a deterministic sensitivity analysis assuming 100% of such patients would receive lifelong rehabilitation therapy, which showed it had a minor impact on base-case results.Fig. 7In conclusion, MenB IMD is an uncommon but severe disease that, from a societal perspective, is associated with a high degree of economic burden on the Spanish health system. The elevated cost per case of MenB-related IMD reflects the severity of the disease, especially for young children among whom the incidence is notably high, in addition to the development of long-term sequelae with associated substantial direct and indirect costs that also affect patients' families and caregivers. elaborates on the findings in a form that could be shared with patients by health care professionals.

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Data sharing

GSK makes available anonymised individual participant data and associated documents from interventional clinical studies, which evaluate medicines, upon approval of proposals submitted to www.clinicalstudydatarequest.com. To access data for other types of GSK sponsored research, for study documents without patient-level data and for clinical studies not listed, please submit an enquiry via the website.

Author contributions

All authors participated in the design, implementation, analysis or interpretation of the study and the development of this manuscript. All authors had full access to the data and gave final approval before submission.

Declaration of competing interest

Declaration of competing interest LAV-A, MT, RR, EdeG, MdelCG-I and JS are employees of the GSK group of companies

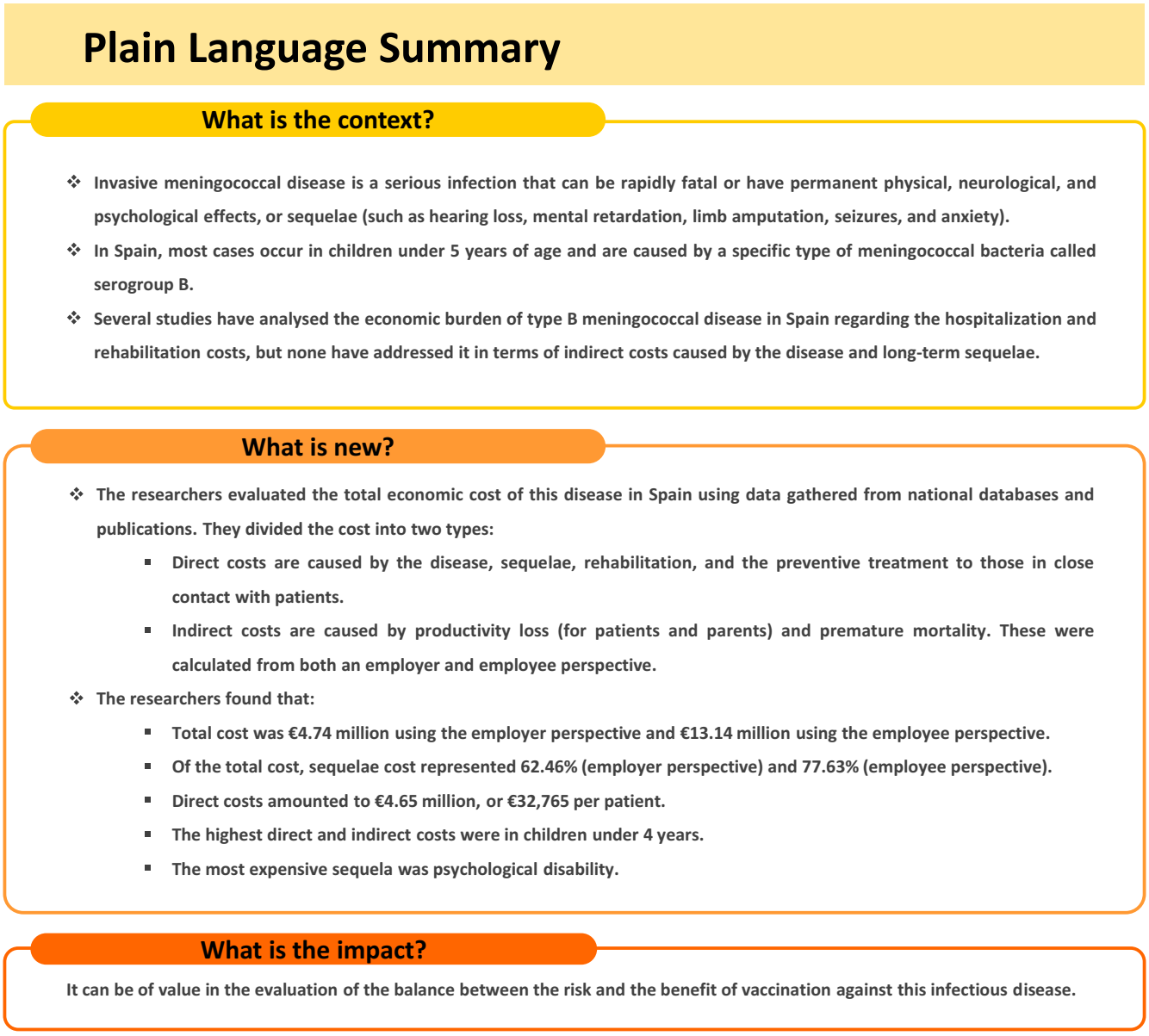

Fig. 7. Plain language summary.

and hold shares of the GSK group of companies. AG is an employee of the GSK group of companies. YI, RS, AG and AH are employees of Weber (Madrid, Spain). Weber received payments from the GSK group of companies for the conduction of the study related to this work. NG-A and AJG-R are employees of the University of Málaga. The University of Málaga received payments from the GSK group of companies for the conduction of the study related to this work. NB is an employee of Aspida, Surrey, UK, and is a complementary worker of the GSK group of companies, on behalf of GSK. All authors declare no other financial or non-financial relationships and activities.

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Appendix A. Supplementary material

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