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Lifetime cost of meningococcal disease in France: Scenarios of severe meningitis and septicemia with purpura fulminans

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Summary Invasive meningococcal disease (IMD) is life-threatening and can result in severe sequelae. In France, no data have been published on the costs of severe IMD cases. Two realistic scenarios were developed with national experts (clinicians and social workers): a 6-year-old child with *purpura fulminans* with amputation of both legs below the knee (case A) and a 3-year-old with meningitis and severe neurological sequelae (case B). Additional scenarios included other typical sequelae of IMD such as chronic kidney disease (CKD), profound deafness and epilepsy. Data on healthcare, disability, educational and other resource use were obtained from experts and families of patients with similar sequelae. Unit costs (2013) were mainly obtained from the literature and the National Health Insurance (NHI). Time horizon was based on life expectancies of patients (77 and 55 years, respectively). A 4% discount rate decreasing to 2% after 30 years was applied. Costs are presented from the perspective of the NHI, publicly funded organizations and patients' families or their private health insurances. *purpura fulminans* with amputations is associated with a lifelong discounted cost of €768,875. Adding CKD doubles the amount (€1,480,545). Meningitis with severe neuro-cognitive sequelae results in a lifelong discounted cost of €1,924,475. Adding profound deafness and epilepsy slightly increases the total cost (€2,267,251). The first year is the most expensive in both scenarios (€166,890

Abbreviations: CKD, chronic kidney disease; IMD, invasive meningococcal disease; MRF, Meningitis Research Foundation; NHI, National Health Insurance; PICU, Pediatric Intensive Care Unit.

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and €160,647 respectively). The main cost drivers for each scenario are prostheses and child/adult stays in healthcare facilities, respectively. Overall, patients' families or his private insurance had to pay around 13% of total cost (101,833€ and 258,817€, respectively). This study fills a gap in the body of knowledge on IMD sequelae care and lifetime costs in France. The potentially high economic burden of IMD, in addition to its physical, psychological and social burden, reinforces the need for prevention.

Introduction

Invasive meningococcal disease (IMD) is a severe bacterial infection caused by *Neisseria meningitidis* or meningococcus, the most disease-associated serogroups being A, B, C, W and Y. Young non-immunized children are the most at risk of contracting the disease. IMD can present as meningococcal septicemia, which can evolve to *purpura fulminans*, very serious septic shock or meningitis [1]. The disease can result in severe sequelae and is fatal in 50—80% of cases if not treated [2—4]. Even when treated, 5—10% of the patients die 24—48 h after the onset of symptoms [2]. This rate is even higher for patients with *purpura fulminans* (15—30%) [5,6]. Sequelae include cerebral lesions, hearing loss, learning difficulties in 10—20% of survivors, deafness in 3—15% and severe cognitive deficits, cerebral palsy or epilepsy in rare cases (3—4%) [7,8]. Of the initial survivors, 10—30% present with skin necrosis and limb ischemia requiring orthopedic surgical management, such as debridement, skin grafting, muscular flap coverage for limb salvage and sometimes even limb amputation [6].

The introduction of meningococcal conjugate vaccines in the last 20 years has resulted in a reduction in the incidence of IMD across Europe [5].

In France, the incidence of IMD has been stable for the last 25 years and is approximately 1 case per 100,000 inhabitants. There is a high predominance of serogroup B (58%) and C (26%) [9], and the incidence of IMD in France remains relatively high compared to other European countries such as Italy or Germany. The very first vaccine to protect against different strains of serogroup B meningococcal bacteria, Bexsero®, became a licensed product in January 2013 and is indicated for children 2 months of age in Europe. More recently in the USA, the FDA granted a license to Bexsero® and to another vaccine Trumenba®, both of which are indicated for those 10—25 years of age. At the time of writing, the UK is the only European country [10] to have started vaccinating infants against serogroup B disease as part of children's routine immunization schedule.

To date, very little data have been published concerning the financial impact of IMD, and no data are available for France, particularly in regards to the different payer perspectives throughout a patient's lifetime. Therefore, we specifically designed this study to estimate the cost of exhaustive resource consumption of two severe and realistic scenarios of IMD cases and their sequelae in France, from the onset of symptoms to the end of life, from all payers' perspectives.

Materials and methods

Scenario development

We developed two scenarios of severe IMD cases: a 6-year-old boy with *purpura fulminans* resulting in amputation of both legs below the knee (case A) and a 3-year-old girl with meningitis resulting in severe neurological sequelae (case B). Additional scenarios were created to include other common sequelae of IMD. Scenarios were initially based on those previously selected in a UK study [11] and were then adapted to France with the help of national experts. Various healthcare specialists (pediatricians, orthopedic surgeons, neurosurgeons, physical therapists, nephrologists, otolaryngologists, prosthesis specialists, social workers, occupational therapists, psychomotor specialists, and independent living specialist) and families of patients with sequelae similar to those of patients A and B were interviewed to describe and evaluate patient management. In total, 19 healthcare professionals, 5 patient's families and one patient group agreed to participate in face-to-face or telephone meetings. Lifelong patient management was described in the interviews and all resource use associated with each step of management was collected. For each family, hypothetical revenues, type of home and distance from home to healthcare professionals were determined. The time horizon was based

Table 1 Costs included in the analysis.

Type of cost	Resources
Direct medical costs	Consultations Transports Hospitalizations Rehabilitation center Drugs Prostheses, wheelchairs, crutches, pressure garments, medicalized stroller, support corset, cochlear implants, diapers
Indirect medical costs (prevention for contacts and social expenses)	Biological tests Blood sampling Public health doctor salary Chemoprophylaxis Vaccines and drugs Accommodation for parents Accommodation and car adaptation Salary of personal assistant Salary of educational assistant Pediatric residential unit Full-time residential care
Indirect costs	Mother's revenue loss Financial aids

on life expectancy estimates (respectively 77 and 55 years for cases A and B).

Costs

All costs are expressed in euros (€) based on their 2013 value. Direct medical and non-medical costs as well as indirect costs were included (Table 1). Income loss was calculated for the parents only, and productivity loss due to the patients' lifetime disability was not included. The costs were discounted according to the methodological guide for health economic evaluation provided by the French National Authority for Health (Haute Autorité de Santé, HAS) [12]. Accordingly, a 4% discount rate that decreased to 2% after 30 years was applied.

The cost of resource consumption was calculated using French cost repositories and was mainly obtained from the literature and National Health Insurance (NHI) data.

Analyses

For each scenario, the following outcomes were estimated by type of expense and by type of payer:

- discounted and undiscounted total cost of IMD from symptom onset to patient death, and
- discounted and undiscounted annual mean cost.

Sensitivity analyses were performed for parameters in which there was uncertainty using lower and upper boundary estimates. Analyses were performed from the perspective of the NHI, publicly funded organizations and patients or their private health insurances.

Results

Patient A

Case A

Patient A contracted IMD with *purpura fulminans* at 6 years old, experiencing fever and a skin rash. After a first outpatient visit with a pediatrician, he was transported by ambulance to the nearest hospital. After several examinations, he was transferred by helicopter to the nearest university hospital, where he was cared for in the Pediatric Intensive Care Unit (PICU) for septic shock associated with respiratory distress syndrome requiring mechanical ventilation. He had necrosis of the limb extremities, which led to amputation of both legs below the knees. After a 1-month stay at the PICU, the patient was transferred to the pediatric ward where he stayed for an additional month while undergoing skin debridement operations and dressing changes. During his stay, his parents stayed in the hospital's Parents House.

Blood analysis was performed to identify the bacterium responsible for the infection. After the serogroup C meningococcus was identified, chemoprophylaxis was prescribed to close contacts of the patient (primary school, family and friends) to avoid bacterial transmission and development of other cases. Additionally, these close contacts were vaccinated with a tetravalent A, C, Y, W135 conjugate vaccine.

After being discharged from the hospital, patient A was transferred to a rehabilitation center for 4 months, which he attended 5 days a week, where he was cared for by an occupational therapist. Once his wounds started to heal, patient A received skin grafts to repair the dermatologic damage on his remaining limbs, which required an additional 1-week hospital stay. Additionally, once the amputated areas were healed, the patient began to receive specialized equipment. A file at the Departmental House for Disability (Maison Départementale du Handicap, MDPH) was created for the patient to obtain financial aid for the costs of care and support that were not reimbursed by public health insurance through the Disability Compensation (Prestation Compensatoire du Handicap, PCH).

The rehabilitative care physician also prepared a report to provide evidence of chronic disease (Affection Longue Durée, ALD), which enabled the patient to receive a 100% reimbursement for his medical care.

After patient A returned home, the pediatrician coordinated his care and visits to specialist health professionals (e.g., physiatrist, orthopedic surgeon, orthoprosthetist, physical therapist, and psychomotor specialist). A home helper was employed for 3 months. Daily nursing care was continued at home because of the patient's superficial necrosis. Additionally, his skin grafts were associated with receiving physical therapy. Patient A underwent two subsequent operations because of post-amputation complications (bone overgrowth from stump). Prostheses were regularly reviewed and replaced to correspond to patient's growth and the evolution of his needs. Liners and sockets were regularly replaced. The patient required crutches and a manual wheelchair for mobility. Additionally, pressure garments following skin grafts were necessary for 2 years. He was active and needed a sports wheelchair throughout his life. Patient A was absent from school during his 6-month hospitalization and went back to school with an educational assistant until he entered secondary school. A taxi that was paid for by the Region Council provided his transport between home and school. Transportation between the rehabilitation center and the patient's home was included in the daily cost of the rehabilitation center. Finally, the transportation expenses associated with visiting health professionals that were made by the patient's family car or by taxi were covered by the NHI.

Patient A was one of 3 children in a two-parent household. Before becoming ill, his mother used to work full-time and earned the minimum French salary; his father was also working full-time and earned the mean French salary. When patient A became ill, his mother stopped working for 6 months, after which she worked part-time. Because of their financial situation, the patient's family benefited from parental leave payments for 6 months and then from basic Handicapped Child Education Aid (Allocation d'Education de l'Enfant Handicapé, AEEH) payments until the patient turned 20 years old. At 18 years old, patient A continued his studies for 3 more years. At 21 years old, he found full-time work in an office and lived independently. A home helper visited him for 7 h each week. He retired at 55 and died at 77.

An alternative scenario was created in which patient A developed chronic kidney disease (CKD) after the episode of *purpura fulminans*, which worsened after several years and required hemodialysis. In this scenario, patient A needed 4 kidney transplants throughout his life.

Costs related to case A

The total discounted cost was €768,875 (lower bound: €585,025; upper bound: €959,964) (Table 2). With the addition of acute kidney injury resulting in CKD to the initial scenario, which required repeated renal grafts throughout the patient's life, the total discounted cost doubled from €768,875 to €1,480,546.

In the initial scenario, the most important driver of cost was the cost of the prostheses (€281,595; 36.6%). Half of the total discounted cost was covered by the NHI (€394,501; 51.3%). The next largest percentage of the total cost was covered by publicly funded organizations (€272,541; 35.4%), followed by the patient's family and/or its private insurance (€101,833; 13.2%). The main expense for the NHI was the cost of the prostheses (€281,595; 71.4%), whereas it was child education for the publicly funded organizations (€100,315; 36.9%) and parents' revenue loss for the patient and/or private insurance (€55,661; 54.7%).

In the occurrence of kidney disease, the largest proportion of the total cost was covered by the NHI (€1,106,033; 74.7%), followed by publicly funded organizations (€272,541; 18.4%) and by the patient's family and/or private insurance (€101,972; 6.9%). Most of the additional costs related to kidney disease were paid for by the NHI.

The mean annual discounted total cost was €10,679 (lower bound: €8125; upper bound: €13,333). The first year represented 21.7% of the total cost and was the year with the highest cost (€166,890) because of the initial hospitalization, rehabilitative care and purchase of specialized equipment (Fig. 1). When acute kidney injury and CKD were added, the mean annual discounted cost totaled €20,563 (lower bound: €18,010; upper bound: €23,217).

Patient B

Case B

Patient B contracted bacterial meningitis at 3 years old, suffering fever, petechiae and loss of consciousness. After a first consultation with a pediatrician, she was transported by ambulance to the nearest university hospital, where she was cared for in the PICU, managed hemodynamically and mechanically ventilated. However, patient B started to convulse and presented with severe encephalitic complications. This resulted in cognitive deficiencies, complete hemiplegia, lateral homonymous hemianopsia, behavioral disorder and

Table 2 Costs (€) according to category for patient A.

Category	NHI	Publicly funded organizations	Patient and private insurance	Total
Prostheses	281,595	0	0	281,595
Specialized equipment	11,867	78,810	19,084	109,760
Education	0	100,315	0.00	100,315
Home help	0	69,735	12,364	82,099
Revenue loss	0	21,553	55,661	77,214
Hospital care	49,354	1325	8016	58,694
Rehabilitative care	28,050	400	2311	30,761
Ambulatory care	23,636	404	4398	28,437
Total discounted cost	**394,501**	**272,541**	**101,833**	**768,875**
Total non-discounted cost	739,547	540,812	173,134	1,453,492
Alternative (CKD) scenario discounted cost	**1,106,033**	**272,541**	**101,972**	**1,480,546**
Alternative (CKD) scenario non-discounted cost	2,655,462	540,812	173,284	3,369,558

Table 3 Costs (€) according to category for patient B.

Category	NHI	Publicly funded organizations	Patient and private insurance	Total
Hospital care	38,373	634	6954	45,961
Rehabilitative care	34,358	500	2797	37,655
Shunt revision	15,506	0	123	15,630
Ambulatory care	8613	2486	7824	18,923
Special equipment	34,697	39,446	56,517	130,660
Education	835,922	0	0	835,922
Revenue loss	0	29,135	130,110	159,244
Home help	0	8719	2453	11,172
Full-time residential care	0	617,269	52,039	669,308
Total discounted cost	**967,469**	**698,189**	**258,817**	**1,924,475**
Total non-discounted cost	1,364,589	2,110,105	447,163	3,921,587
Alternative scenario discounted cost	**1,339,029**	**659,324**	**268,898**	**2,267,251**
Alternative scenario non-discounted	2,126,648	1,984,828	467,741	4,579,218

hydrocephalus. The latter was treated by the insertion of a ventriculoperitoneal shunt. After a 1-month stay in the PICU, the patient was transferred to the pediatric ward where she stayed for an additional month. During her stay at the hospital, her parents stayed in the hospital's Parents House.

Blood analysis was performed to identify the bacterium responsible for the infection. The serogroup W135 meningococcus was identified, and chemoprophylaxis was prescribed to close contacts of the patient (nursery school, family and friends) to avoid bacterial transmission and development of other cases. Additionally, these close contacts were vaccinated with a tetravalent A, C, Y, W135 conjugate vaccine.

Once discharged from the hospital, patient B was transferred to a rehabilitation center for 5 months, which she attended 5 days a week, where she was cared for by an occupational therapist. She also consulted a neurosurgeon for follow-up for her ventriculoperitoneal shunt. Regular surgical revisions of the ventriculoperitoneal shunt were required throughout the patient's life. A file at the MDPH was created for the patient to obtain financial aid

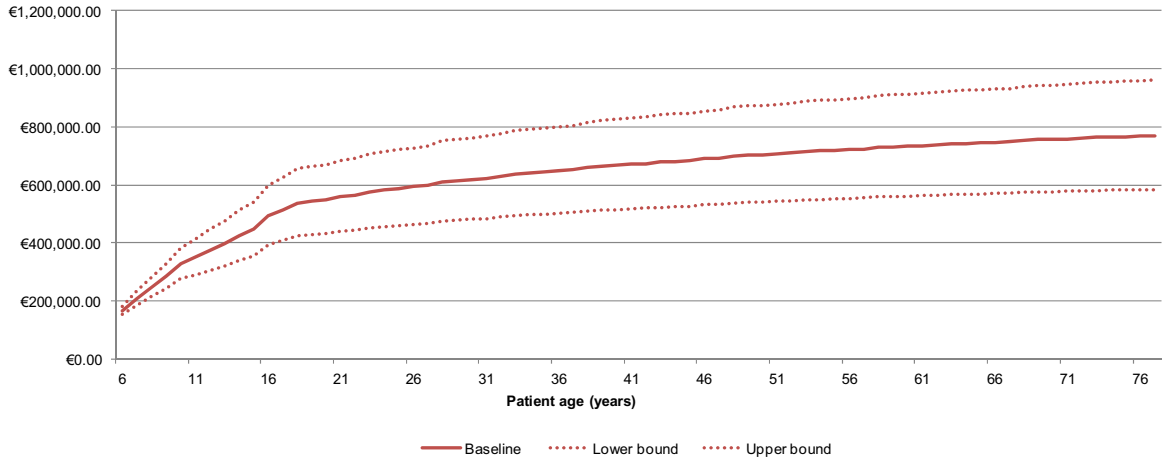

Figure 1 Cumulative discounted lifelong costs (case A).

for the care and support that was not reimbursed by public health insurance through the PCH. The rehabilitative care physician also prepared a report to provide evidence of chronic disease in order for the patient to claim a 100% reimbursement for medical care.

Once the patient had returned home, her pediatrician coordinated her care and visits to specialist health professionals (physical therapist, psychomotor specialist, occupational therapist, etc.). A home helper was employed for 17 months. As patient B was unable to walk, she had an electric wheelchair and a medical stroller, which were replaced when she was 5 years old by a manual wheelchair. She had a support trunk corset during growth. Patient B was in substantial pain, resulting in daily doses of analgesic medication. Additionally, cerebral lesions led to her becoming incontinent. Patient B was sent to a specialist school called the Medical-Educational Institute (Institut Médico-Educatif, IME) from age 5 to 20. Transportation between the rehabilitation center or IME and the patient's home was included in the daily cost of the rehabilitation center. Transportation from the patient's home to health professional visits was provided by the patient's parents, and the expenses were covered by the NHI.

Patient B was one of 2 children in a two-parent household. Her mother and father worked full-time and both earned the mean French salary. When patient B became ill, her mother stopped working for 7 months and then returned to work part-time until her child was 20 years old. Because of their financial situation, the family benefited from parental leave payments for 6 months and then received basic Handicapped Child Education Aid until the patient was 20 years old. When patient B turned 20 years old, she was placed in full-time residential care. She died at 55.

In an alternative scenario, patient B also had pharmacologically treated epilepsy and profound deafness. She was followed by a neurologist. Her epileptic episodes consisted of an acute epileptic attack 3 times a year requiring hospitalization for each attack. Her pharmacological treatment led to treatment-induced constipation, and she initiated treatment with a constipation drug. Patient B's profound deafness required both cochlear implants (one in each ear), which were implanted during the acute phase, as well as regular consultations with the surgeon and speech specialist. The external part of the implant was replaced every 5 years.

Costs related to case B

The total discounted cost was €1,924,475 in the scenario without epilepsy or deafness (lower bound: €1,279,617; upper bound: €2,740,387) (Table 3). With the addition of epilepsy and deafness, the total discounted cost increased slightly from €1,924,475 to €2,267,251.

In the initial scenario, the most important cost driver was the cost of education (€835,922; 43.4%), followed by the cost of full-time residential care (€669,308; 34.8%). The NHI covered the largest proportion of the total cost (€967,469; 50.3%), followed by publicly funded organizations (€698,189; 36.3%) and by the patient's family and/or private insurance (€258,817; 13.4%). For the NHI, the cost of education was the main expense (€835,922; 86.4%) (of note, IME costs are 100% reimbursed). For publicly funded organizations, full-time residential care was the main expense (€617,269; 88.4%), and for the patient's family and private insurance, the parents' revenue loss was the main expense (€130,110; 50.3%).

In the scenario in which the patient experienced epilepsy and deafness, more than half of the total

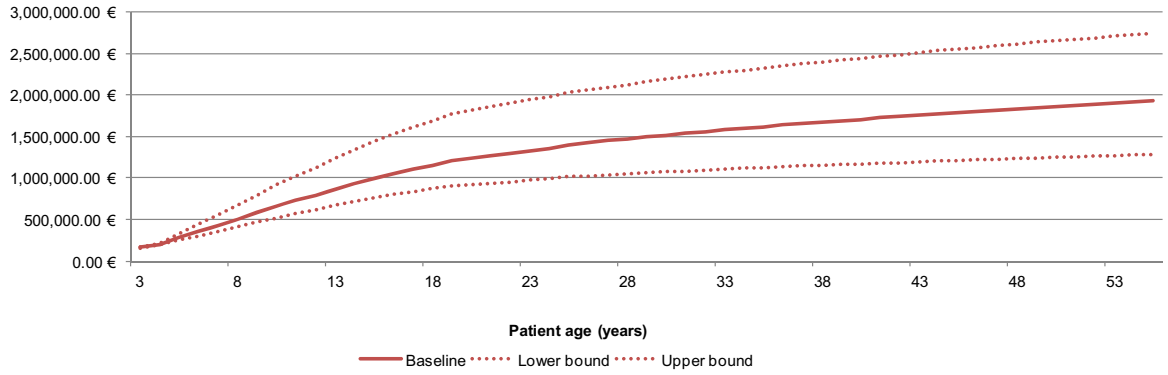

Figure 2 Cumulative discounted lifelong costs (case B).

cost was covered by the NHI (€1,339,029; 59.1%), the publicly funded organizations covered the next largest proportion of the total cost (€659,324; 29.1%), followed by the patient and/or private insurance (€268,898; 11.9%).

The mean annual discounted total cost was €36,311 (lower bound: €24,144; upper bound: €51,705). The first year represented 8.3% of the total cost and was the year with the highest cost (€160,648) because of the initial hospitalization, rehabilitative care and purchase of specialized equipment (Fig. 2). When epilepsy and deafness were added to the scenario, the mean annual discounted cost total totaled €42,778 (lower bound: €30,503; upper bound: €58,065).

Discussion

Overall, a severe case of IMD with *purpura fulminans* and leg amputation was estimated to be associated with a lifelong discounted cost of approximately €770,000 in France. If the consequences were more serious, such as if kidney injury/disease occurred due to *purpura fulminans*, the total discounted cost more than doubled to €1.5 million. In our study, a case of IMD with severe neurological sequelae resulted in a lifelong discounted cost of €1,924,475 in France. Adding profound deafness and epilepsy increased this cost to €2,267,251. This study also showed that resource consumption was greater in the year following the onset of symptoms; our results indicated that the costs totaled about €160,000 for the first year regardless of the type of IMD. The NHI covered approximately half of the total cost of care regardless of the case studied (case A or case B), publicly funded organizations one third and the patient or private insurance covered the remaining cost. The main driver of cost was the prostheses in the case of *purpura fulminans* and the pediatric and full-time residential care in the case of meningitis with severe neurological sequelae.

This study is the first to estimate the costs associated with lifelong IMD in France and was conducted in response to an identified need for which the scientific literature did not supply adequate information. The study methodology was adapted from that of a study performed in the UK in 2013 by the Meningitis Research Foundation (MRF), and the results of this study are consistent with theirs, although the costs were slightly lower. Indeed, they estimated that the total discounted cost to the UK government of a severe case of IMD over 70 years would be £1,360,000 to £1,720,000 [11]. The MRF also estimated severe IMD cases to be associated with a cost of £160,000 to £200,000 in the first year for the NHI/Personal Social Services (PSS), while we estimated these costs to be €160,000. These differences may partly be explained by the slightly less severe nature of the cases in our study (i.e., in our study the patient with *purpura fulminans* was 6 years old and had both legs amputated below the knee, whereas the MRF study described a 10-month-old with one arm and both legs amputated above the knee) and the shorter time horizons (71 and 52 years in scenarios A and B, respectively, versus 70 years in the English study). A similar study has also been conducted in Spain using the same methodology [13]. The results of the Spanish study showed a total cost of €1,200,000 and €1,400,000 over 70 years. They estimated that IMD cases are associated with a cost of €197,000 and €155,000 in the first year.

This study has several strengths. The methodology used is that of the MRF, which enables comparison of the results. Cases A and B were adapted and validated by national experts in the management of IMD and the management of disability. Moreover, the sequelae described in the

scenarios reflect what has been observed, as shown in a recent literature review [14].

A detailed cost study was performed to incorporate all of the costs associated with the management of IMD. Total costs were explored from different perspectives and were discounted to reduce the impact of events that occur further in the future, in accordance with the recommendations for the good practice of health-economics in France. Sensitivity analyses were conducted to estimate the uncertainty concerning the main results, given the variability in unit costs. Thus, the results of this study can be used by health economists and modelers in full cost-effectiveness evaluations to better represent the lifetime costs of treating severe disease.

Nonetheless, our study has some limitations. The costs of CKD were obtained from the Blotière et al. study published in 2010 [15]. However, little information about the cost was provided in this study, which could potentially have led to a slight underestimation of certain costs. Finally, some costs were not included in our study as they were very difficult to measure (e.g., child care for other children in the family during consultations and hospitalizations or indirect costs related to loss of patient autonomy).

Although the severity of IMD varies greatly from one case to another, from complete recovery to very severe sequelae, which explains the difficulty in evaluating the cost of IMD, this study fills a gap in the body of knowledge on the care and costs of IMD and its sequelae. Our study shows that the management of such patients is burdensome in terms of disability and expenditure for health insurance, families and government agencies. Given the financial impact of IMD and its sequelae, this study emphasizes the fact that it is important to include all of the health dimensions (acute disease, sequelae) and to adopt all of the perspectives within health-economic evaluations when designing prevention strategies for IMD.

Although the incidence of IMD in France remains stable, it is important to maintain a policy to prevent IMD through informational campaigns and vaccination programs. Recently, the first vaccine with broad-spectrum protection against serogroup B meningococcus has been approved in Europe, which represents an opportunity to significantly decrease the burden of severe IMD cases.

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Competing interests

None declared.

Ethical approval

Not required.

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References

[1] Parent du Chatelet I, Taha MK, Lepoutre A, Maine C, Deghmane AE, Lévy-Bruhl D. Les infections invasives à méningocoques en France en 2010. Bull Epidémiol Hebd 2011;45—46:475—80.
[2] World Health Organization. Aide-mémoire N°141; 2012, November. www.who.int/mediacentre/factsheets/fs141/fr/index.html [accessed February 2013].
[3] Flexner S. The results of the serum treatment in thirteen hundred cases of epidemic meningitis. J Exp Med 1913;17(5):553—76.
[4] Swartz MN. Bacterial meningitis—a view of the past 90 years. N Engl J Med 2004;351(18):1826—8.
[5] Institut national de veille sanitaire. Guide pratique sur la conduite à tenir devant un ou plusieurs cas d'infection invasive à meningocoque; 2011, January. http://circulaire.legifrance.gouv.fr/pdf/2011/02/cir_32603.pdf [accessed February 2013].
[6] Nectoux E, Mezel A, Raux S, Fron D, Maillet M, Herbaux B. Meningococcal purpura fulminans in children: I. Initial orthopedic management. J Child Orthop 2010;4(October (5)):401—7.
[7] Des Portes V. Quel suivi à long terme pour quels patients? Séquelles des méningites bactériennes chez l'enfant et chez l'adulte: incidence, types, modes d'évaluation. Med Mal Inf 2009;39(7—8):572—80.
[8] Viner RM, Booy R, Johnson H, Edmunds WJ, Hudson L, Bedford H, et al. Outcomes of invasive meningococcal serogroup B disease in children and adolescents (MOSAIC): a case—control study. Lancet Neurol 2012;11(September (9)):774—83.
[9] Institut national de veille sanitaire. Epidemiological data; 2014, September. http://www.invs.sante.fr/Dossiers-thematiques/Maladies-infectieuses/Maladies-a-prevention-vaccinale/Infections-invasives-a-meningocoques/Donnees-epidemiologiques [accessed November 2014].
[10] Letter from Public Health England — Introduction of MenB immunisation for infants. https://www.gov.uk/government/publications/menb-vaccination-introduction-from-1-september-2015.

[11] Wright C, Wordsworth R, Glennie L. Counting the cost of meningoccal disease. Pediatr Drugs 2013;15(February (1)):49—58.
[12] Haute Autorité de Santé. Choix méthodologiques pour l'évaluation économique à la HAS; 2011, October. http://www.has-sante.fr/portail/upload/docs/application/pdf/2011-11/guide_methodo_vf.pdf [accessed November 2014].
[13] Darbà J, Kaskens L, Hark M, Wright C. Costs of surviving meningococcal disease in Spain: evaluation for two cases of severe meningitis and septicaemia. Vaccine 2014; 32(September (39)):5006—12.
[14] Vyse A, Anonychuk A, Jäkel A, Wieffer H, Nadel S. The burden and impact of severe and long-term sequelae of meningococcal disease. Expert Rev Anti Infect Ther 2013;11(June (6)):597—604.
[15] Blotière PO, Tuppin P, Weill A, Ricordeau P, Allemand H. Coût de la prise en charge de l'IRCT en France en 2007 et impact potentiel d'une augmentation du recours à la dialyse péritonéale et à la greffe. Nephrol Ther 2010;6(4):240—7.