

# Healthcare and productivity loss costs in young adults after bacterial meningitis: a cross-sectional follow-up study

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## ABSTRACT

**Objective** To determine healthcare and productivity loss costs among young adult survivors of childhood bacterial meningitis (BM).

**Methods** In this cross-sectional study, online versions of the Institute for Medical Technological Assessment (iMTA) Medical Consumption Questionnaire and the iMTA Productivity Costs Questionnaire were used to measure healthcare consumption and productivity loss costs in young adult survivors of childhood BM. Mean healthcare and productivity loss costs were calculated and the differences in costs across subgroups based on age at onset, sex and causative pathogens were investigated.

**Results** A total of 454 patients were included in the cost analysis of healthcare utilisation and a total of 471 patients were included in the cost analysis of productivity losses. The 3-month mean societal cost per patient amounted to €4985.32 (median €1363.71, IQR €576.04–€2948.67), of which €4790.84 (median €1125.90, IQR €271.20–€2489.54) was due to productivity losses. Productivity loss costs were significantly higher in survivors of childhood BM caused by *Streptococcus pneumoniae* compared with survivors of childhood BM caused by *Neisseria meningitidis*.

**Conclusions** This study highlights the potential significant economic burden in young survivors of childhood BM and emphasises the possible impact of very long-term sequelae. In particular, very long-term sequelae of BM contribute to indirect costs. To the best of our knowledge, this is the first study to investigate the societal costs of childhood BM over a two-decade follow-up period. Further research into societal costs in young adult survivors of neonatal meningitis is needed to provide additional insights into the economic burden of childhood BM.

## INTRODUCTION

Acute bacterial meningitis (BM) during childhood is a severe, much-feared disease with substantial mortality and morbidity.<sup>1–3</sup> Incidence rates of community-acquired BM range from approximately 0.9 per 100 000 individuals per year in high-income countries to 80 per 100 000 individuals per year in low-income countries.<sup>3,4</sup> In low-income countries, BM has

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Bacterial meningitis (BM) is a severe disease with a high economic burden owing to its substantial mortality and morbidity. Very long-term sequelae in survivors of childhood BM may not be recognised or reported, leading to an underestimation of the actual economic burden.

## WHAT THIS STUDY ADDS

⇒ The present study provides new insights on societal costs and contributes to bridging the existing data gap by estimating these costs in two large, unique cohorts of young adult survivors of childhood BM. It is the first study in the Netherlands two decades after onset of the disease.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Incorporating these data into cost-effectiveness analyses and global burden estimates will guide policymakers and health organisations in making informed decisions regarding surveillance and prevention.

a mortality rate of up to 54%. According to morbidity, the risk of neurological sequelae such as focal neurological deficits (eg, hemiparesis, hearing loss and cognitive impairment) varies, with rates ranging from 9.4% in Europe to 25% in Africa.<sup>3,5</sup> Over the past three decades, conjugate vaccines targeting specific serogroups or serotypes of disease-causing pathogens have been developed and incorporated into routine paediatric vaccination programmes. Consequently, case fatality rates have declined due to improved prevention efforts, along with enhanced treatment and surveillance strategies.<sup>2,3,6</sup> However, the meningitis burden remains high and progress lags substantially behind that of other vaccine-preventable diseases.<sup>3,7</sup>

Burden of disease (BOD) studies specifically assess the ‘burden’ in terms of years of

life lost due to premature death, as well as years lived with disability or morbidity (YLD).<sup>8</sup> These two components form a measure known as total disability-adjusted life-years (DALYs), which reflects both healthcare costs and the 'lost economic or societal contributions' resulting from premature death or disability.<sup>8</sup> Globally in 2016, 1.48million (95% UI (UI: uncertainty intervals defined by 25th and 975th draw values (sampling of 1000)) 1.04–1.96) YLDs were due to meningitis compared with 21.87million (95% UI 18.20–28.28) DALYs. *Streptococcus pneumoniae* was responsible for the highest number of YLDs (95% UI: 634 458 (444 787–839 749)), showing severe long-term effects on survivors.<sup>2</sup> The accumulated disability burden was estimated to be the highest in adolescents and young adults, with sequelae such as cognitive disability, epilepsy, vision impairment and motor impairment.<sup>2</sup> 54% (1.53million (95% UI 1.23–1.95)) of incident cases and 46% (146 322 (95% UI 114 583–216 388)) of all deaths occurred in children younger than 5 years and risk of neurological disability was highest under 1 year of age.<sup>2</sup>

Unfortunately, the relative paucity of data on distribution and severity of long-term sequelae in survivors in BOD studies leads to burden underestimation and hinders progress towards the comprehensive vision outlined in the 2030 roadmap, 'Towards a World Free of Meningitis'.<sup>1</sup> This roadmap has set three ambitious goals: the elimination of BM epidemics, a 50% reduction in cases of vaccine-preventable BM, a 70% reduction in deaths and a reduction in disability and improvement in quality of life for those affected by meningitis, regardless of the cause.

In light of this goal and the existing data gap, the present study aimed to estimate the costs of healthcare and productivity loss in two large, unique cohorts of young adult survivors of childhood BM. These data can be used in cost-effectiveness analyses for vaccines and global economic burden studies, aiding in decision-making in vaccine implementation. To our knowledge, this is the first study in the Netherlands to estimate societal costs more than two decades after childhood BM.

## METHODS

This study was embedded in the Dutch 20130 Postmeningitis Study in which two cohorts of patients with childhood BM were invited for the present study.<sup>9</sup> Both cohorts used in the 20130 Postmeningitis Study were retrospectively selected from data on bacterial cerebrospinal fluid (CSF) isolates from the Netherlands Reference Laboratory for Bacterial Meningitis. These patients were originating from hundred and ten different Dutch hospitals. The first cohort consisted of 628 children born between January 1986 and December 1994 who survived non-Haemophilus type B meningitis between January 1990 and December 1995.<sup>10</sup> 586 survivors from the first cohort were included due to the inability to retrieve all address details from the local authority registers. The

second cohort consisted of 361 children born between January 1993 and December 1999 who survived non-Haemophilus type B meningitis between January 1997 and December 2001.<sup>11</sup> Survivors of haemophilus type B meningitis were excluded due to the declining incidence of the disease during the cohort selection, as a result of vaccination efforts.

BM was diagnosed based on the isolation of bacteria from CSF. The exclusion criteria included a complex onset of meningitis (defined as meningitis secondary to immunodeficiency states, central nervous system surgery, cranial trauma and CSF shunt infections of relapsing meningitis). Patients from both original cohorts who consented for future follow-up studies were invited to participate in the present single-centre study.

## Data collection

Data on costs due to productivity losses and healthcare consumption were collected through two online questionnaires. A link was provided to eligible participants with an explanation on how to complete the online questionnaires. Before completing the questionnaires, the participants were asked to sign an online informed consent form. Data on productivity losses and healthcare consumption in the present study were collected digitally between April 2018 and October 2019. Only participants who completed all the questionnaires were included in this study.

## Main outcome measures

Cost estimation was derived using the following three steps:

### Identification

Costs included were categorised as: healthcare costs (ie, medical procedures), patient and family costs (ie, travel costs) and costs in other sectors (ie, productivity costs). As there were no registrations available for time and travel costs, those costs were excluded.

### Measurement

Self-reported questionnaires for healthcare consumption and productivity losses were used in this study.

The Institute for Medical Technological Assessment (iMTA) Productivity Costs Questionnaire was used to measure indirect costs outside the healthcare sector, also known as productivity costs.<sup>12</sup> Within productivity costs, a distinction is made between productivity losses within paid work due to absenteeism, presenteeism and productivity losses within unpaid work.<sup>13–15</sup> A recall period of 4 weeks was used and these costs were extrapolated to 3 months.<sup>1 2</sup> The iMTA Medical Consumption Questionnaire (iMCQ) was used to measure direct costs within the healthcare sector.<sup>16</sup> The iMCQ was developed to obtain consistent and standardised information on healthcare consumption. A recall period of 3 months was used.<sup>17 18</sup> The items in both questionnaires are not related to any disease or specific disorder and are commonly used in

the Netherlands to assess healthcare and productivity losses.

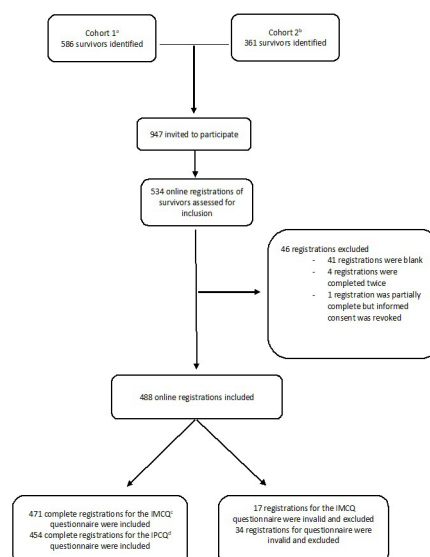
### Valuation

The costs were expressed and analysed in euros and indexed for 2017. The updated Dutch Manual for Cost Analysis in Health Care Research was used to evaluate the healthcare costs.<sup>19</sup> The health services identified and used by the patients were multiplied by their corresponding unit prices. Total costs were calculated by summing the individual services. All medication costs were derived from the website with the official listing of drugs with prices: [www.medicijnenkosten.nl](http://www.medicijnenkosten.nl). Medication costs were based on the price per dosage of the drug in the Netherlands.

Productivity losses were valued using the friction cost approach (FCA), which accounts for production losses confined to the period needed to replace the sick employee (85 days=12 weeks).<sup>17</sup> For example, in the case of a short absence: a person works 32 hours per week, spread over 4 days per week. The respondent has been absent for 2 days in the past 4 weeks. The productivity losses are then calculated as follows: 2 days×8 hours per workday×€34.75 = €556. In case of long absence (duration shorter than the friction period): a person works 24 hours per week, spread over 3 days per week. Based on the start date of the absence, the total duration of the absence is calculated to be 56 (calendar) days. The productivity losses are then calculated as follows: 56 calendar days of absence=56/7=8 working weeks. 8 working weeks×3 working days per week=24 working days. 24 working days×8 hours per workday×€34.75=€6672. In case of long absence (duration longer than the friction period): A person works 24 hours per week, spread over 3 days per week. Based on the start date of the absence, the total duration of the absence is calculated to be 100 (calendar) days. The productivity costs are limited to the friction period (85 days). The productivity losses are then calculated as follows: 85 calendar days of absence=85/7=12.1 working weeks. 12.1 working weeks×3 working days per week=36.3 working days. 36.3 working days×8 hours per workday×€34.75=€10 091.40.

### Statistical analyses

All statistical analyses were performed using IBM SPSS Statistics for Windows, V.28 (IBM). Since the cost data were highly skewed, non-parametric bootstrapping (with 5000 replications) was used to estimate the 95% CIs around the mean difference in all cost categories. Subgroup analyses were performed according to the age at onset, sex and causative pathogens that were investigated. Differences between the two independent groups were evaluated using the Mann-Whitney U test. Linear regression analyses were performed to control for potential confounding factors (times since diagnosis (years), current age (years), age at onset (months) and causative pathogen). The first analysis included total healthcare costs as dependent variable and gender as independent



**Figure 1** Flow chart demonstrating the selection of participants for the Dutch 20/30 Postmeningitis Study. <sup>a</sup>Koomen I, Grobbee DE, Jennekens-Schinkel A, Roord JJ, van Furth AM. Parental perception of educational, behavioural and general health problems in school-age survivors of bacterial meningitis. *Acta Paediatr.* 2003;92(2):177–85. <sup>b</sup>de Jonge RC, Sanders MS, Terwee CB, Heymans MW, Gemke RJ, Koomen I, *et al* Unsuccessful validation of model for predicting academic or behavioural limitations after childhood bacterial meningitis. *Acta Paediatr.* 2013;102(12):e553–9. <sup>c</sup>iMTA Medical Consumption Questionnaire (iMCQ). <sup>d</sup>iMTA Productivity Cost Questionnaire (iPCQ). iMTA, institute for medical technological assessment.

variable. The second analysis included productivity loss costs as the dependent variable and with gender as the independent variable.

### Patient and public involvement

Patients or the public did not partake in the design, conduct, reporting or dissemination plans of this research.

### RESULTS

A total of 488 participants were included in the Dutch 20/30 Postmeningitis Study after deduplication and exclusion of participants who did not fill in any of the questionnaires, and a subsample of 471 participants fully completed the iMCQ. The iMTA Productivity Cost Questionnaire was fully completed by 454 participants (see figure 1). Demographic and clinical characteristics are reported in table 1. A total of 164 (33.6%) survivors of childhood BM had a high educational level (at least higher vocational education), and 410 (84.0%) survivors reported paid employment. Unpaid employment was not due to education but mainly due to complaints or specific daily activities for survivors suffering from intellectual disability. Differences in demographic and clinical characteristics between survivors of childhood BM who did not participate or were excluded in Dutch 20/30

**Table 1** Demographic and clinical characteristics of childhood meningitis survivors (N=471)

| Gender                                                                                                      |                     |
|-------------------------------------------------------------------------------------------------------------|---------------------|
| Male, n %                                                                                                   | 209 (43)            |
| Age, median IQR                                                                                             | 25.15 (18.00–32.00) |
| Age at onset ≤12 months, n %                                                                                | 147 (31)            |
| Time since meningitis, median IQR                                                                           | 22.43 (7.00–32.00)  |
| Special needs in school, n %                                                                                | 171 (36)            |
| Grade repeated in school, n %                                                                               | 171 (36)            |
| Survivors with sequelae*, n %                                                                               | 125 (27)            |
| Causative pathogen                                                                                          |                     |
| <i>Neisseria meningitidis</i> , n %                                                                         | 369 (78)            |
| <i>Streptococcus pneumoniae</i> , n %                                                                       | 94 (20)             |
| Other: <i>Listeria monocytogenes</i> ,<br><i>Escherichia coli</i> and <i>Streptococcus agalactiae</i> , n % | 8 (2)               |
| Dexamethasone during admission, n %                                                                         | 98 (21)             |
| Employment status                                                                                           |                     |
| Unemployed, n %                                                                                             | 61 (13)             |
| Poor health-related quality of life†, n %                                                                   | 47 (10)             |
| Overall quality of life score‡, mean SD                                                                     | 3.80 (0.88)         |

\*Sequelae included: hearing impairment (defined as unilateral or bilateral perceptive loss of >25 dB), intellectual disability, epilepsy, paresis, focal neurology, ataxia, vision loss, cognitive impairment.  
†The Dutch version of the PROMIS-GH V.1.2: T-score on global mental health scales of <38 and T-score on global physical health scales of <35.  
‡The Dutch version of the PROMIS-GH V.1.2: Global 02, overall quality of life: 5-point Likert scale, ranging from 1 indicating 'poor overall quality of life' to 5 indicating 'very good quality of life'.

Postmeningitis Study and the survivors of childhood BM included in the present study were not significant.

The mean societal cost per survivor of childhood BM amounted to €4985.32 (median €1363.71, IQR €576.04–€2948.67) over a period of 3 months of which 96.1% (€4790.84 median €1125.90, IQR €271.20–€2489.54) was due to productivity losses. (table 2). Mean total healthcare costs represented 4.9% (€194.48 median 33.00, IQR €0–€197.36) of the total societal costs. The main contributors to healthcare costs were visits to allied health professionals; emergency room visits; visits to outpatient clinics and treatment procedures (table 2). 30% of the total healthcare costs were related to sequelae (eg, costs of supportive devices due to hearing impairment/cognitive impairment). 51 survivors of childhood BM were unable to perform unpaid labour for 361.2 hours (median 15, IQR 6.00–40.00) (45 days) (table 2). 50% of productivity loss costs were related to sequelae (eg, inability to work due to persistent cognitive and hearing impairment and behaviour disorders (mainly attention deficit disorder/attention-deficit/hyperactivity disorder).

### Difference in societal costs across subgroups according to gender and age at onset

Table 3 presents the differences in costs according to sex and age at onset. Female survivors of childhood BM incurred significantly higher total healthcare costs (€57.29, IQR €0–€264.00) than did male survivors (€0, IQR €0–€99.00) ( $p<0.001$ ). Among individual healthcare costs, the mean treatment costs were also significantly higher for women (€690.00, IQR €276.00–€1276.50) than for men (€276.00, IQR €141.50–€414.00) ( $p=0.040$ ). Additionally, the mean societal costs were considerably higher for women (€1319.90, IQR €570.00–€2905.75) than for men (€1501.20, IQR €582.20–€3445.66) ( $p<0.0001$ ). The mean total productivity loss costs were €1158.33 (IQR €289.58–€2704.07) for women and €1073.25 (IQR €235.80–€2365.74) for men, but this difference was not statistically significant ( $p=0.721$ ). No statistically significant differences in costs were found between survivors of childhood BM with an onset age below 12 months and those with an onset age above 12 months.

### Difference in societal costs across subgroups according to causative pathogen

Table 4 shows differences in costs by causing pathogens of *S. pneumoniae* versus *Neisseria meningitidis* (NM). The mean productivity loss costs and mean societal costs were significantly higher for survivors of childhood BM caused by *S. pneumoniae* (€834.00, IQR €272.20–€1563.75 vs €1142.10, IQR €285.19–€2970.19,  $p=0.001$  and €1261.59, IQR €792.00–€2522.70, respectively, vs €1366.02, IQR €545.21–€3508.36  $p=0.001$ ). The mean costs for medications were also significantly higher for survivors of childhood BM caused by *S. pneumoniae* (€23.32 (IQR €7.41–€151.97) vs €6.14 (IQR €2.04–€37.79),  $p=0.015$ ). No other statistically significant differences in costs were observed between patients with meningitis caused by *S. pneumoniae* and those with meningitis caused by NM.

### Regression analyses controlling for confounding factors

The linear regression analyses revealed no confounding effects from time since diagnosis, age at onset, current age or causative pathogen on productivity loss and total healthcare costs (see online supplemental tables 1,2).

## DISCUSSION

The present study aimed to provide insight into the societal costs of young adult survivors of childhood BM. The majority of the costs in our study were indirect costs, primarily due to productivity losses among young adult survivors of childhood BM. The 3-month mean societal cost per patient amounted to €4985.32 (median €1363.71, IQR €576.04–€2948.67) of which €4790.84 (median €1125.90, IQR €271.20–€2489.54) was due to productivity losses. Thus, indirect costs account for a substantial portion of total costs. 30% of the healthcare

**Table 2** Total resource use and costs (euros)

| Resource use per patient       | Cost per patient (€) |          |        |         |         |          |         |                 |
|--------------------------------|----------------------|----------|--------|---------|---------|----------|---------|-----------------|
|                                | N                    | Per cent | Mean   | SD      | Mean    | SD       | Median  | 95% CI          |
| General practitioner           | 172                  | 38.00    | 1.62   | 0.486   | 64.27   | 45.60    | 33.00   | (57 to 71)      |
| Medications                    | 119                  | 38.00    | 126.37 | 220.53  | 71.08   | 14.64    | 9.10    | (43 to 101)     |
| Outpatient clinic              | 61                   | 12.50    | 2.39   | 2.25    | 222.28  | 206.32   | 182.00  | (174 to 278)    |
| Allied health professionals    | 130                  |          | 5.14   | 4.79    | 245.49  | 244.91   | 132     | (205 to 288)    |
| Homecare                       | 1                    | 0.002    | 65.00  | –       | 260.00  | –        | –       | –               |
| Hospital stay                  | 5                    | 1.00     | 1.20   | 0.48    | 13.63   | 142.55   | 0.00    | (2, 28)         |
| Emergency room visits          | 19                   | 3.90     | 0.06   | 0.30    | 340.79  | 194.06   | 259.00  | (272 to 436.21) |
| Ambulance                      | 3                    | 0.60     | 0.01   | 0.08    | 0.34    | 4.218    | 0       | (0 to 6)        |
| Diagnostics                    | 5                    | 1.02     | 1.80   | 0.45    | 31.83   | 21.22    | 21.22   | (21 to 53)      |
| Treatment                      | 14                   | 3.1      | 2.68   | 2.40    | 690.71  | 665.14   | 552.00  | (405 to 1058)   |
| Total healthcare costs         | 454                  | 100      |        |         | 194.48  | 404.91   | 33.00   | (159 to 235)    |
| Inability due to unpaid labour | 51                   | 10.50    | 361.18 | 2016.46 | 8307.06 | 46378.76 | 345.00  | (896 to 2.2963) |
| Total productivity loss costs  | 145                  | 30.79    |        |         | 4790.84 | 27598.24 | 1125.90 | (2019 to 9784)  |
| Societal costs                 |                      |          |        |         | 4985.32 | 15943.10 | 67.30   | (834 to 3372)   |

Units per resource: general practitioner, outpatient clinic, allied health professionals, emergency room visits: contact; Medications: various; Homecare; inability due to unpaid labour: hour; hospital stay: nightstay; ambulance trip; treatment: procedure.

costs were associated with sequelae, while 50% of the productivity loss costs were linked to sequelae. Total healthcare costs per patient were €194.48 (median 33.00, IQR €0–€197.36) and represented 4.9% of societal costs. The majority of healthcare expenditures, including consultations with allied health professionals, emergency room visits and treatments such as antibiotics and other supportive therapies. No previous studies have provided specific quantified data on total healthcare costs and productivity losses in young adult survivors of childhood

BM in the Netherlands. However, there are a lot of costs of illness studies on invasive meningococcal disease and invasive pneumococcal disease.<sup>17 19–21</sup> Zeevat *et al* recently estimated the economic burden of MenB-related invasive meningococcal disease in the Netherlands between 2015 and 2019.<sup>18</sup> Sequelae were responsible for 81% of the direct costs/case. The differences in percentages of healthcare costs related to sequelae between our study and the mentioned studies might be explained by the fact that our study was conducted cross-sectionally, 23 years

**Table 3** Costs (expressed in euros) of childhood bacterial meningitis patients according to sex and age\*

|                                | Male (N=209) |         |                | Female (N=262) |         |                | P value          |
|--------------------------------|--------------|---------|----------------|----------------|---------|----------------|------------------|
|                                | N            | Median  | IQR            | N              | Median  | IQR            |                  |
| General practitioner           | 61           | 33.00   | 33.00–66.00    | 111            | 66.00   | 33.00–99.00    | 0.462            |
| Medications                    | 46           | 6.04    | 1.07–87.41     | 73             | 12.74   | 4.03–46.38     | 0.222            |
| Outpatient clinic              | 23           | 182.00  | 91.00–273.00   | 38             | 244.86  | 136.50–273.00  | 0.926            |
| Allied health professionals    | 40           | 131.00  | 66.00–310.50   | 90             | 160.50  | 66.00–343.500  | 0.519            |
| Hospital stay                  | 2            | 0       | 0              | 3              | 0       | 0              | 0.865            |
| Emergency room visits          | 10           | 259.00  | 259.00         | 9              | 259.00  | 259.00–518.00  | 0.497            |
| Ambulance                      | 2            | 0.52    | 52.00          | 1              | 0       | 0              | 0.424            |
| Diagnostics                    | 3            | 42.44   | 21.22–63.66    | 2              | 21.22   | 21.22          | 1.000            |
| Treatment                      | 4            | 276.00  | 143.50–414.00  | 10             | 690.00  | 276.00–1276.50 | <b>0.040</b>     |
| Total healthcare costs         | 199          | 0       | 0.00–99.00     | 145            | 57.29   | 0–264.00       | <b>&lt;0.001</b> |
| Inability due to unpaid labour | 51           | 345.00  | 576.05–2948.67 | 39             | 368.00  | 138.00–1150.00 | 0.730            |
| Total productivity loss costs  | 145          | 1125.90 | 271.21–2489.55 | 101            | 1158.33 | 289.58–2704.07 | 0.721            |
| Societal costs                 | 44           | 1501.20 | 582.00–3445.66 | 101            | 1319.90 | 570.00–2905.75 | <b>&lt;0.001</b> |

Bold values indicate Cost categories with significant p-value.

\*See online supplemental material for complete table. Homecare was excluded from analysis due to n=1.

**Table 4** Costs (expressed in euros) of childhood bacterial meningitis patients according to causing pathogen\*

|                                | Streptococcus pneumoniae patients (N=94) |         |                | Neisseria meningitidis patients (N=369) |         |                | P value      |
|--------------------------------|------------------------------------------|---------|----------------|-----------------------------------------|---------|----------------|--------------|
|                                | N                                        | Median  | IQR            | N                                       | Median  | IQR            |              |
| General practitioner           | 36                                       | 66.00   | 33.00–99.00    | 129                                     | 33.00   | 33.00–66.00    | 0.293        |
| Medications                    | 28                                       | 23.32   | 7.41–151.97    | 81                                      | 6.14    | 2.04–37.79     | <b>0.015</b> |
| Outpatient clinic              |                                          | 91.00   | 91.00–182.00   |                                         | 182.00  | 91.00–273.00   | 0.073        |
| Allied health professionals    | 25                                       | 104.00  | 64.50–354.00   | 97                                      | 150.00  | 70.50–320.00   | 0.281        |
| Hospital stay                  | 0                                        | 0       | 0              | 5                                       | 0       | 0              | –            |
| Emergency room visits          | 6                                        | 259.00  | 0–259.00       | 11                                      | 259.00  | 259.00–518.00  | 0.256        |
| Ambulance                      | 2                                        | 0       | 52.00          | 1                                       | 0       | 52.00          |              |
| Diagnostics                    | 1                                        | 21.22   | 21.22          | 2                                       | 42.44   | 42.44          | 0.667        |
| Treatment                      | 3                                        | 276.00  | 817.39         | 11                                      | 552.00  | 276.00–1104.00 | 0.368        |
| Total healthcare costs         | 33                                       | 33.00   | 0–287.95       | 346                                     | 33.00   | 0–165.00       | 0.816        |
| Inability due to unpaid labour | 11                                       | 207.00  | 115.00–460.00  | 38                                      | 414.00  | 155.25–1184.54 | 0.164        |
| Total productivity loss costs  | 21                                       | 834.00  | 272.20–1563.75 | 112                                     | 1142.10 | 285.19–2970.19 | <b>0.001</b> |
| Societal costs                 | 21                                       | 1261.58 | 792.00–2522.70 | 112                                     | 1366.02 | 545.21–3508.36 | <b>0.001</b> |

Bold values indicate Cost categories with significant p-value.

\*Patients with neonatal meningitis caused by *Listeria monocytogenes*, *Streptococcus agalactiae*, *Escherichia coli* were excluded from analysis due small numbers. Homecare was excluded from analysis due to n=1.

after meningitis and did not include the costs from the acute phase. A shift in the percentage of costs associated with sequelae is expected; however, it is interesting to note that productivity costs remain substantial in young adult survivors, with at least half of these costs linked to sequelae. Additionally, our study obviously focused on meningitis and the study population was selected to investigate subtle residual sequelae, which could lead to underestimation of healthcare costs and productivity losses related to more severe sequelae.

Pickering *et al* estimated healthcare costs 10 years after meningitis caused by NM in a prospective cohort study that included 340 Danish survivors with onset of NM meningitis in childhood and adolescence. Healthcare costs were significantly higher at disease onset and the following year, but thereafter were the same as that of controls and amounted to approximately €1700 in total and €5 per survivor. The difference in healthcare costs compared with our study might be due to the time period, calculation method and the fact that our cohort also included survivors of pneumococcal meningitis.<sup>22</sup>

Significant research has focused on the direct healthcare costs of invasive pneumococcal disease, primarily to assess vaccine efficacy.<sup>20 23–25</sup> As a result, most existing cost-effectiveness analyses emphasise the costs associated with the acute phase of the disease, such as hospitalisation, antibiotic treatment and direct medical interventions. These studies are not directly comparable to our study, as they focus on short-term healthcare expenditures, whereas our study aimed to explore long-term societal costs for young adult survivors. Nevertheless, Mohanty *et al* recently demonstrated that work ability is significantly

reduced in adults diagnosed with BM during childhood, particularly among survivors of pneumococcal meningitis.<sup>26</sup> These results support our findings, specifically regarding productivity losses.<sup>27</sup> More research is needed to assess the societal costs of childhood pneumococcal meningitis survivors. This is particularly necessary given the global increase in the proportion of pneumococcal meningitis cases in recent years, along with the decreased but persistent high case-fatality rate. In addition, *S. pneumoniae* is the leading cause of BM among children aged 0–4 years in the Netherlands, responsible for 30% of all meningitis cases,<sup>28</sup> further emphasising its significance.

Survivors of childhood BM caused by *S. agalactiae*, *E. coli* and *L. monocytogenes*—considered as neonatal meningitis—were excluded from the analysis in the present study due to small sample sizes. Puhó *et al*<sup>29</sup> observed higher healthcare utilisation among children with invasive group B streptococcal disease compared with unexposed children. Since infants under 3 months of age have the highest incidence of BM across all age groups, further research is needed to provide a more comprehensive understanding of the economic burden of childhood BM.<sup>29</sup>

Although our study provides valuable insights into the societal costs associated with BM, it is important to consider some limitations. First, we did not incorporate societal costs during the acute phase, which limits our understanding of how these costs change over time. Second, we did not account for additional indirect costs, such as transportation and out-of-pocket expenses, potentially leading to an underestimation of the total costs. Moreover, using an online testing procedure, which may

have restricted the participation of patients with more severe sequelae, could also have led to underestimation of costs.

Third, the lack of an unexposed comparison cohort and the use of non-registered data may introduce both selection and confounding biases. Finally, variations in valuation methodology—using the FCA versus the human capital approach (HCA)—influence the estimated total costs. In the HCA, productivity costs associated with premature death are calculated based on the loss of future economic production over the expected remaining lifetime, adjusted for age and gender. The FCA as an alternative method, stating that, when unemployment is high, indirect costs due to work absence estimated with the FCA may be lower than with the HCA.<sup>28</sup> This occurs for several reasons: (1) diminishing marginal returns to labour; (2) short-term absences can be replaced by internal labour reserves; (3) individuals can compensate for lost productivity once they return to work and (4) non-urgent tasks can be cancelled.<sup>28</sup> To fully estimate productivity costs using FCA, information is needed on: (1) when a friction period begins; (2) the length of the friction period; (3) an estimate of production loss, with particular attention to the elasticity of production; (4) the costs of searching for and training replacement workers and (5) medium-term macroeconomic effects.<sup>28</sup> In our study, we used FCA to calculate productivity costs, as FCA is officially recognised in the Netherlands as the most accurate approximation of the real costs to society.<sup>28 30</sup>

## CONCLUSIONS

The findings of this study highlight the potential significant financial burden in young adult survivors of childhood BM, particularly due to productivity losses. Survivors of meningitis caused by *S. pneumoniae*, in particular, may experience high long-term costs. Given the variations in costs associated with different pathogens, further research into the societal costs for adolescent and young adult survivors of neonatal meningitis and how these costs change over time is needed to provide additional insight into the economic burden of childhood BM.

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## REFERENCES

- 1 Priya V. World Health Organization Defeating meningitis by 2030. *Lancet Infect Dis* 2021;21:1635.
- 2 Zunt JR, Kassebaum NJ, Blake N, *et al*. Global, regional, and national burden of meningitis, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2018;17:1061–82.
- 3 van Ettekovon CN, Liechti FD, Brouwer MC, *et al*. Global Case Fatality of Bacterial Meningitis During an 80-Year Period: A Systematic Review and Meta-Analysis. *JAMA Netw Open* 2024;7:e2424802.
- 4 Bijlsma MW, Brouwer MC, Kassenmoentalib ES, *et al*. Community-acquired bacterial meningitis in adults in the Netherlands, 2006–14: a prospective cohort study. *Lancet Infect Dis* 2016;16:339–47.
- 5 Edmond K, Clark A, Korczak VS, *et al*. Global and regional risk of disabling sequelae from bacterial meningitis: a systematic review and meta-analysis. *Lancet Infect Dis* 2010;10:317–28.
- 6 Wright C, Blake N, Glennie L, *et al*. The Global Burden of Meningitis in Children: Challenges with Interpreting Global Health Estimates. *Microorganisms* 2021;9:377.
- 7 Koelman DLH, van Kassel MN, Bijlsma MW, *et al*. Changing Epidemiology of Bacterial Meningitis Since Introduction of Conjugate Vaccines: 3 Decades of National Meningitis Surveillance in The Netherlands. *Clin Infect Dis* 2021;73:e1099–107.
- 8 Polinder S, Haagsma JA, Stein C, *et al*. Systematic review of general burden of disease studies using disability-adjusted life years. *Popul Health Metr* 2012;10:21.
- 9 El Tahir O, de Jonge RCJ, Ouburg S, *et al*. Study protocol: The Dutch 20130 Postmeningitis study: a cross-sectional follow-up of two historical childhood bacterial meningitis cohorts on long-term outcomes. *BMC Pediatr* 2019;19:519.

- 10 Koomen I, Grobbee DE, Roord JJ, *et al.* Hearing loss at school age in survivors of bacterial meningitis: assessment, incidence, and prediction. *Pediatrics* 2003;112:1049–53.
- 11 Koomen I, Raat H, Jennekens-Schinkel A, *et al.* Academic and behavioral limitations and health-related quality of life in school-age survivors of bacterial meningitis. *Qual Life Res* 2005;14:1563–72.
- 12 Bouwmans C, Krol M, Brouwer W, *et al.* IMTA Productivity Cost Questionnaire (IPCQ). *Value Health* 2014;17:S1098-3015(14)03721-8.
- 13 Koopmanschap MA. PRODISQ: a modular questionnaire on productivity and disease for economic evaluation studies. *Expert Rev Pharmacoecon Outcomes Res* 2005;5:23–8.
- 14 Vos JAM, El Aili M, Duineveld LAM, *et al.* Cost-effectiveness of general practitioner- versus surgeon-led colon cancer survivorship care: an economic evaluation alongside a randomised controlled trial. *J Cancer Surviv* 2024;18:1393–402.
- 15 Vervoort VM, Vriesevold JE, Olde Hartman TC, *et al.* Cost of illness and illness perceptions in patients with fibromyalgia. *Clin Exp Rheumatol* 2016;34:S74–82.
- 16 Bouwmans C, Krol M, Severens H, *et al.* The iMTA Productivity Cost Questionnaire: A Standardized Instrument for Measuring and Valuing Health-Related Productivity Losses. *Value Health* 2015;18:753–8.
- 17 Weil-Olivier C, Taha M-K, Emery C, *et al.* Healthcare Resource Consumption and Cost of Invasive Meningococcal Disease in France: A Study of the National Health Insurance Database. *Infect Dis Ther* 2021;10:1607–23.
- 18 Zeevat F, Simons JJM, Westra TA, *et al.* Cost of Illness Analysis of Invasive Meningococcal Disease Caused by Neisseria Meningitidis Serogroup B in the Netherlands-a Holistic Approach. *Infect Dis Ther* 2024;13:481–99.
- 19 Scholz S, Koerber F, Meszaros K, *et al.* The cost-of-illness for invasive meningococcal disease caused by serogroup B Neisseria meningitidis (MenB) in Germany. *Vaccine (Auckl)* 2019;37:1692–701.
- 20 Shiri T, Khan K, Keaney K, *et al.* Pneumococcal Disease: A Systematic Review of Health Utilities, Resource Use, Costs, and Economic Evaluations of Interventions. *Value Health* 2019;22:1329–44.
- 21 Ivanova-Markova Y, González-Domínguez A, Hidalgo A, *et al.* Cost of illness of invasive meningococcal disease caused by serogroup B Neisseria meningitidis in Spain. *Vaccine (Auckl)* 2021;39:7646–54.
- 22 Pickering L, Jennum P, Ibsen R, *et al.* Long-term health and socioeconomic consequences of childhood and adolescent onset of meningococcal meningitis. *Eur J Pediatr* 2018;177:1309–15.
- 23 Adamu AL, Karia B, Bello MM, *et al.* The cost of illness for childhood clinical pneumonia and invasive pneumococcal disease in Nigeria. *BMJ Glob Health* 2022;7:e007080.
- 24 Bardach A, Ruvinsky S, Palermo MC, *et al.* Invasive pneumococcal disease in Latin America and the Caribbean: Serotype distribution, disease burden, and impact of vaccination. A systematic review and meta-analysis. *PLoS One* 2024;19:e0304978.
- 25 Kolhapure S, Yewale V, Agrawal A, *et al.* Invasive Pneumococcal Disease burden and PCV coverage in children under five in Southeast Asia: implications for India. *J Infect Dev Ctries* 2021;15:749–60.
- 26 Mohanty S, Johansson Kostenniemi U, Silfverdal SA, *et al.* Adult Work Ability Following Diagnosis of Bacterial Meningitis in Childhood. *JAMA Netw Open* 2024;7:e2445497.
- 27 Tetens MM, Obel N. Socioeconomic Outcomes Associated With Childhood Bacterial Meningitis-Long-Term Socioeconomic Outcomes Matter to Patients. *JAMA Netw Open* 2024;7:e2445458.
- 28 Pike J, Grosse SD. Friction Cost Estimates of Productivity Costs in Cost-of-Illness Studies in Comparison with Human Capital Estimates: A Review. *Appl Health Econ Health Policy* 2018;16:765–78.
- 29 van der Flier M. Neonatal meningitis: small babies, big problem. *Lancet Child Adolesc Health* 2021;5:386–7.
- 30 Finkelstein EA, Fiebelkorn IC, Wang G. National Medical Spending Attributable To Overweight And Obesity: How Much, And Who's Paying? *Health Aff (Millwood)* 2003;22:W3–219.