

Economic burden of pneumococcal disease among US children — a review of cost-effectiveness analyses of pneumococcal vaccines

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Background

- Pneumococcal disease is a group of conditions with various clinical presentations in children, including invasive pneumococcal disease, pneumonia, and acute otitis media (AOM)
- Invasive pneumococcal disease, specifically meningitis, can lead to long-term debilitating sequelae; 20% of patients with bacterial meningitis experience severe complications¹
- Pneumococcal disease and post-meningitis sequelae could incur substantial health care resource use and costs to the health care system and society
- Costs associated with pneumococcal disease are not only an important measure of disease burden but also used as the key inputs to estimate the cost-effectiveness of pneumococcal vaccines
- Therefore, the accuracy of cost estimates is crucial to our understanding of the economic burden associated with pneumococcal disease and the economic value of pneumococcal vaccines

Objective

- To summarize the costs associated with pneumococcal disease and post-meningitis sequelae in children, based on cost-effectiveness analyses (CEAs) of pediatric pneumococcal vaccines in the US

Methods

- Literature search of CEAs of pediatric pneumococcal vaccines in the US
 - CEAs included in a published systematic literature review (SLR) of economic evaluations of pneumococcal disease² were screened for study eligibility
 - The SLR included all relevant literature up to 2016
 - A targeted literature review was conducted using MEDLINE to identify eligible CEAs published between 2016 and 2023
- In addition, the references in the identified CEAs were screened to identify additional relevant CEAs
- To be included in the study, a CEA must have met the following criteria:
 - Conducted among children in the US
 - Including pneumococcal vaccine as an intervention
 - Reporting at least one cost input associated with pneumococcal disease or post-meningitis sequelae
 - Published between 2000 and 2023
- The source studies from which the cost inputs in the included CEAs were obtained or derived were also reviewed
- Data extraction and evidence synthesis
 - Study characteristics (authors, year published, perspective, and time horizon), base-case cost input values, ranges of cost inputs in the sensitivity analysis, references for cost inputs, and source studies (when available) were extracted from the included CEAs
 - Costs were converted to 2023 US dollars (USD) using the medical component of consumer price index³
 - Ranges of cost inputs were summarized by disease type and age group
 - Sources for cost inputs were also summarized
 - Direct medical costs and direct nonmedical/indirect costs were synthesized separately

Results

Overview of selected CEAs

- Eleven CEA studies published from 2000 to 2023 met the selection criteria and were included in the synthesis (**Table 1**)
 - Disease type
 - Eight CEAs included all pneumococcal diseases, including invasive pneumococcal disease, pneumonia, AOM, and post-meningitis sequelae
 - One CEA included all pneumococcal disease and post-meningitis sequelae types except AOM
 - One CEA included pneumonia and AOM
 - One CEA included AOM only
 - Cost type
 - Nine CEAs took the societal perspective, including both direct medical costs and direct nonmedical/indirect costs
 - Two CEAs used the healthcare perspective and considered direct medical costs only
- Only two studies reported ranges of cost inputs in the sensitivity analysis; thus, this review summarized base-case cost inputs only

Table 1. List of included CEAs

First author	Year	Perspective	Time horizon	Disease(s) considered in the model
Prasad N	2023	Societal	15 years for acute pneumococcal disease; lifetime for sequelae	Invasive pneumococcal disease, pneumonia, AOM, and post-meningitis sequelae
Huang M	2023	Societal	Lifetime	Invasive pneumococcal disease, pneumonia, AOM, and post-meningitis sequelae
Stoecker C	2013	Societal	10 years for acute pneumococcal disease; lifetime for sequelae	Invasive pneumococcal disease, pneumonia, AOM, and post-meningitis sequelae
McGarry LJ	2013	Health care	1 year for acute pneumococcal disease; lifetime for sequelae	Invasive pneumococcal disease, pneumonia, and post-meningitis sequelae
Rubin JL	2010a	Societal	10 years for acute pneumococcal disease; lifetime for sequelae	Invasive pneumococcal disease, pneumonia, AOM, and post-meningitis sequelae
Rubin JL	2010b	Health care	1 year for acute pneumococcal disease; lifetime for sequelae	Invasive pneumococcal disease, pneumonia, AOM, and post-meningitis sequelae
O'Brien MA	2009	Societal	4 years for acute pneumococcal disease; lifetime for sequelae	AOM
Ray GT	2009	Societal	7 years for acute pneumococcal disease; lifetime for sequelae	Invasive pneumococcal disease, pneumonia, AOM, and post-meningitis sequelae
Ray GT	2006	Societal	5 years for acute pneumococcal disease; lifetime for sequelae	Invasive pneumococcal disease, pneumonia, AOM, and post-meningitis sequelae
Lieu TA	2000	Societal	Lifetime	Invasive pneumococcal disease, pneumonia, AOM, and post-meningitis sequelae
Weycker D	2000	Societal	10 years for acute pneumococcal disease	Pneumonia and AOM

Sources for cost inputs (Table 2)

- Most of the included CEAs referenced other CEAs and published or unpublished cost studies for cost inputs; a small proportion of CEAs also used microcosting methods and assumptions to estimate cost inputs
- Sources for direct medical costs
 - Pneumococcal disease
 - The most common sources were other published CEAs, followed by unpublished cost analyses and published original cost studies
 - A total of four published cost studies were referenced
 - Post-meningitis sequelae
 - Over half of the studies referenced other CEAs; the rest referenced three published cost studies
- Sources for direct nonmedical/indirect costs
 - Pneumococcal disease
 - Similar to direct medical costs, the most common sources were other published CEAs
 - Published cost studies were only referenced for AOM-related cost inputs
 - Post-meningitis sequelae
 - The most common sources were published cost studies

Table 2. Summary of CEA studies by cost type, disease type, and data source

Disease type	Number of CEAs	Number of CEAs using the following references ^a					Published original cost studies used ^b
		Other CEAs	Published cost studies	Unpublished cost analyses	Microcosting methods	Assumptions	
Direct medical costs							
Invasive pneumococcal disease	9	6	1	3	1	0	Hu T, 2023
Meningitis	9	6	1	2	0	0	Hu T, 2023
Non-meningitis	9	6	1	2	0	0	Hu T, 2023
Invasive pneumococcal disease (undifferentiated)	4	2	0	1	1	0	—
Pneumonia	10	5	2	4	1	2	Hu T, 2023; Zhou F, 2007
Inpatient pneumonia	7	4	2	2	1	0	Hu T, 2023; Zhou F, 2007
Outpatient pneumonia	6	3	2	1	0	2	Hu T, 2023; Zhou F, 2007
Pneumonia (undifferentiated)	4	2	0	2	0	0	—
AOM	10	5	3	2	1	0	Hu T, 2023; Zhou F, 2008; Capra AM 2000
AOM/simple AOM	10	5	3	2	1	0	Hu T, 2023; Zhou F, 2008; Capra AM 2000
Complex/recurrent AOM	5	2	2	0	1	0	Hu T, 2023; Capra AM 2000
Tube placement	7	2	2	2	1	0	Hu T, 2023; Capra AM 2000
Post-meningitis sequelae	9	5	4	0	0	0	CDC 2004; Waitzman NJ 1996; Severens JL 1997
Disability/neurological deficits	9	5	4	0	0	0	CDC 2004; Waitzman NJ 1996
Deafness/hearing loss	9	5	4	0	0	0	CDC 2004; Severens JL 1997
Direct nonmedical and indirect costs							
Invasive pneumococcal disease	7	6	0	1	1	0	—
Meningitis	7	6	0	1	1	0	—
Non-meningitis	7	6	0	1	1	0	—
Pneumonia	8	7	0	1	1	0	—
Inpatient pneumonia	5	5	0	0	1	0	—
Outpatient pneumonia	5	5	0	0	0	0	—
Pneumonia (undifferentiated)	3	2	0	1	0	0	—
AOM	9	8	2	0	0	1	Capra AM 2000; Lieu TA 1994
AOM/simple AOM	8	8	1	0	0	0	Capra AM 2000; Lieu TA 1994
Complex/recurrent AOM	4	3	1	0	0	0	Capra AM 2000
Tube placement	7	5	1	0	0	1	Capra AM 2000
Post-meningitis sequelae	7	2	5	0	0	0	CDC 2004; Birnbaum HG, 2001; Waitzman NJ 1996
Disability/neurological deficits	7	2	5	0	0	0	CDC 2004; Birnbaum HG, 2001; Waitzman NJ 1996
Deafness/hearing loss	3	0	3	0	0	0	CDC 2004

CEA, cost-effectiveness analysis; AOM, acute otitis media.

^aSome CEAs used multiple references. Therefore, the total number of studies using various references may sum to more than the number of CEAs.

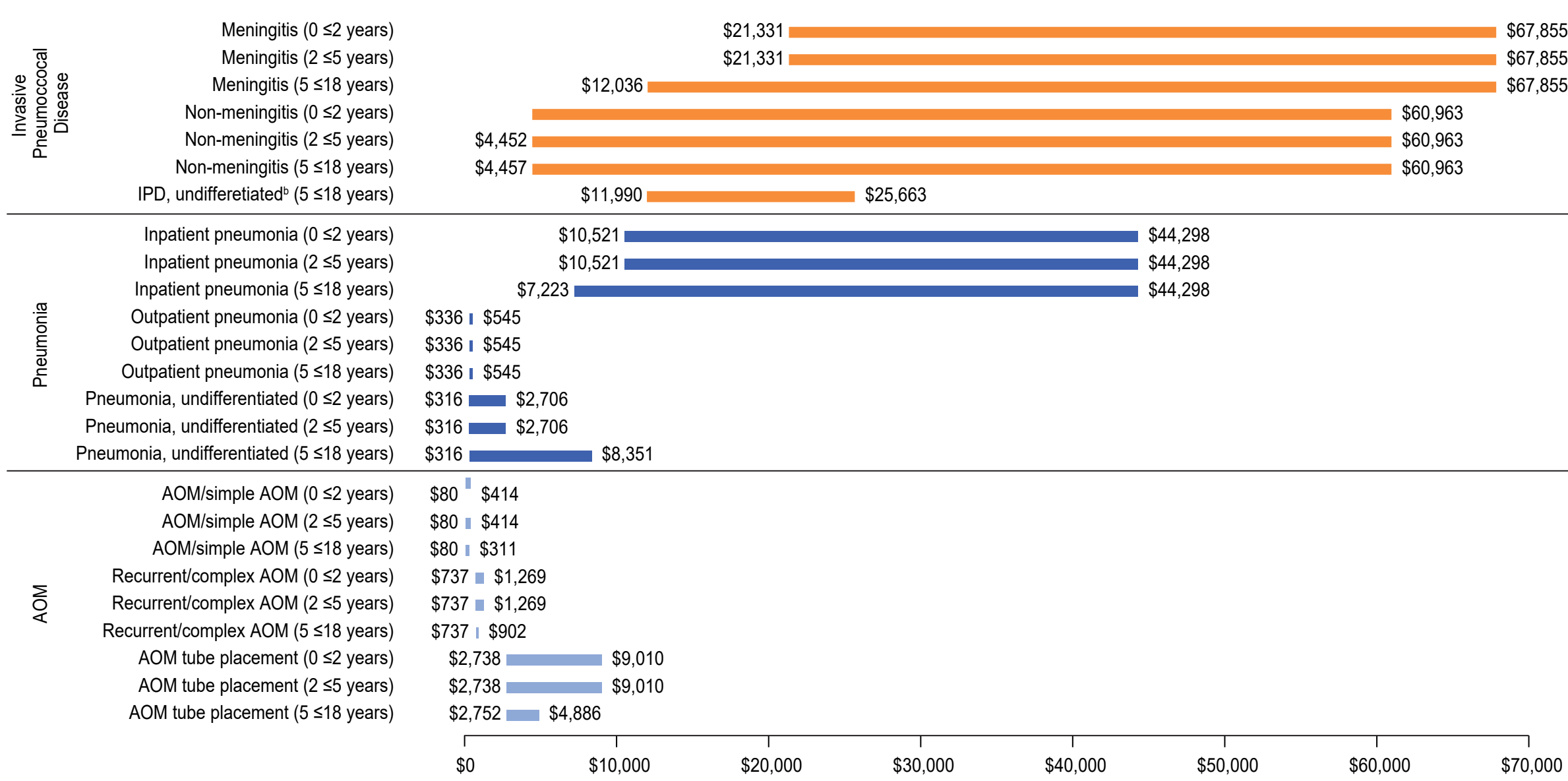
^bNot all CEAs used published cost studies.

Direct medical costs

Cost inputs for pneumococcal disease in included CEAs

- All included CEAs used cost per pneumococcal disease episode, except two CEAs, which also used cost per visit as the inputs for AOM/simple AOM
- Range of cost per episode in the base case is presented in **Figure 1**
 - Overall, meningitis was associated with the highest cost per episode, followed by nonmeningitis invasive pneumococcal disease, and inpatient pneumonia
 - AOM tube placement and undifferentiated pneumonia were also associated with substantial costs per episode
 - Outpatient pneumonia and AOM/simple AOM had the lowest costs per episode among all pneumococcal disease types
 - There were wide ranges in the cost inputs for these conditions
 - Age-specific cost inputs were presented in the CEAs, but they were generally similar across age groups

Figure 1. Direct medical cost per episode of pneumococcal disease^a (2023 USD)



USD, United States dollars; IPD, invasive pneumococcal disease; AOM, acute otitis media.

^aRanges of base-case cost inputs by disease type and age are presented. Depending on the cost input used in the CEA, it may be included in 1 or more age categories.

All costs reported in the CEA were converted to 2023 USD using the medical component of the consumer price index.

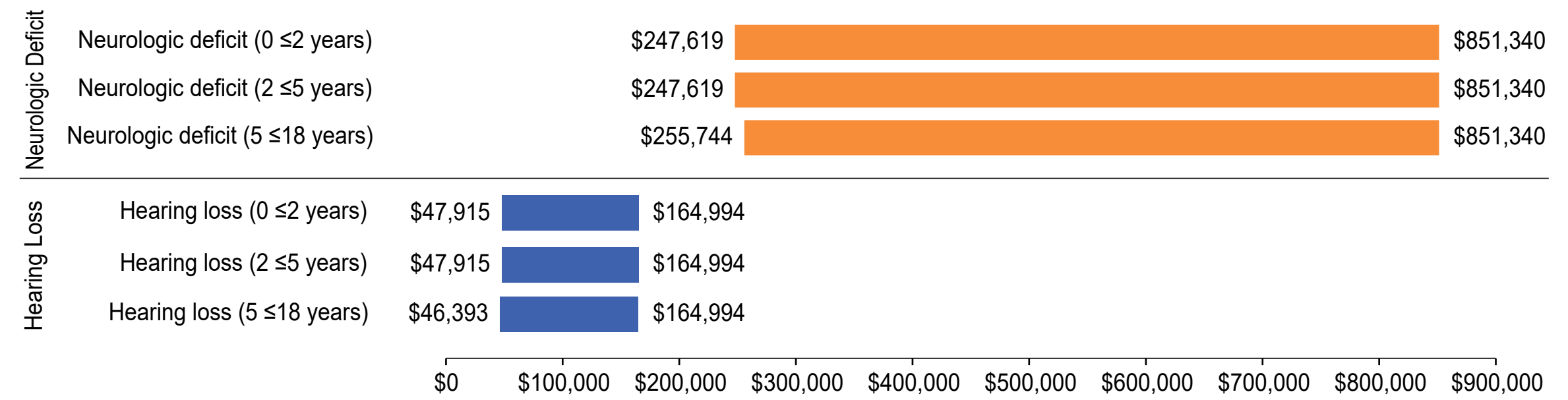
^bCost inputs for invasive pneumococcal disease (undifferentiated) were only available for the age category of 5-18 years.

Direct medical costs

Cost inputs for post-meningitis sequelae in included CEAs

- All CEAs used lifetime costs for post-meningitis sequelae, except one study,⁴ which used annual costs for post-meningitis sequelae; therefore, lifetime costs for post-meningitis sequelae were summarized
- Range of lifetime costs in the base case was presented in **Figure 2**
 - Both neurologic deficit and hearing loss were associated with substantial lifetime economic burden
 - The costs of neurologic deficit were considerably higher than the costs of hearing loss
 - Similar to pneumococcal disease, there were no obvious differences in costs of post-meningitis sequelae across age groups

Figure 2. Lifetime direct medical cost associated with post-meningitis sequelae^a (2023 USD)



^aRanges of base-case cost inputs by disease type and age are presented. Depending on the cost input used in the CEA, it may be included in one or more age categories.

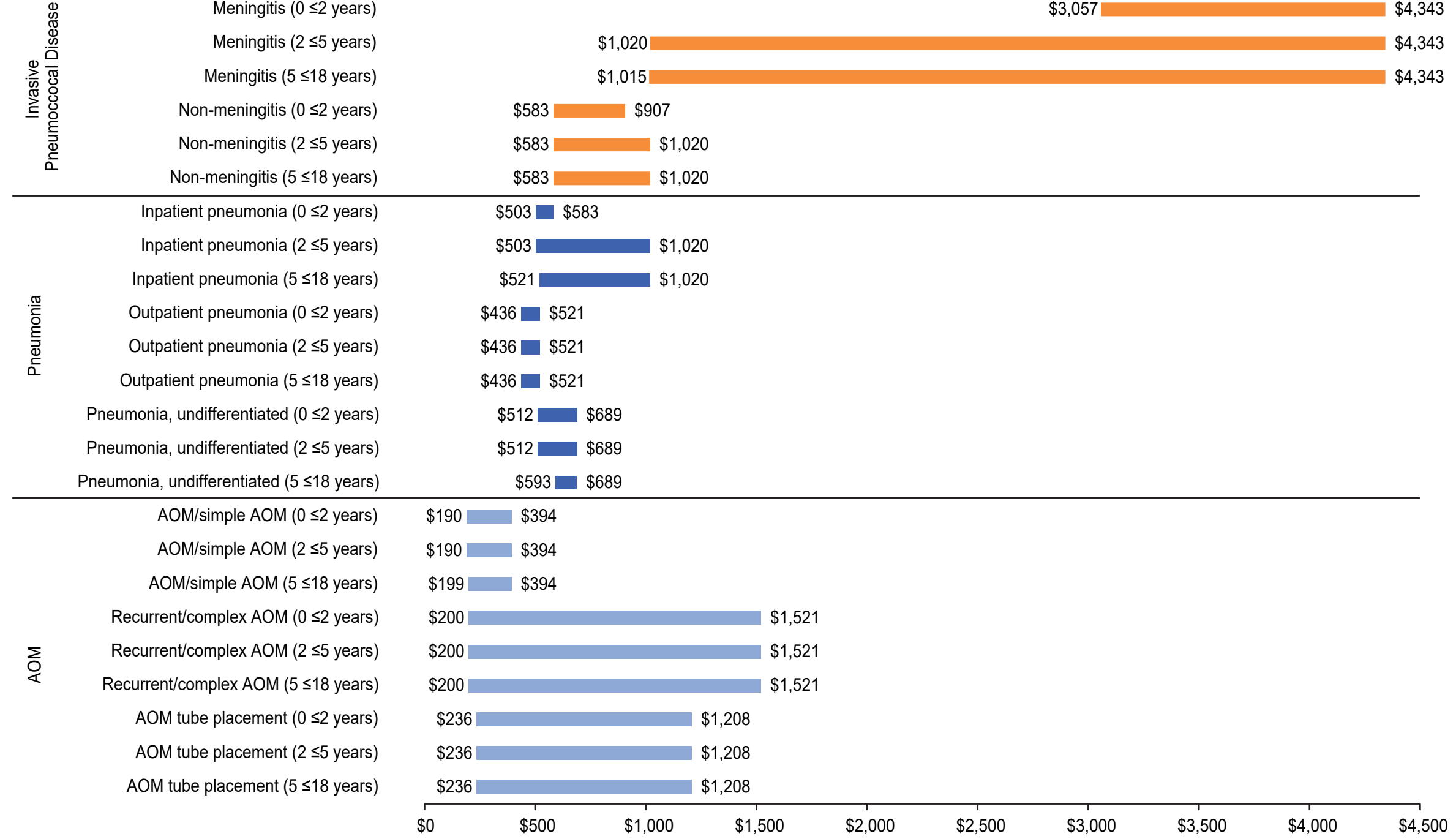
All costs reported in the CEA were converted to 2023 USD using the medical component of the consumer price index.

Direct nonmedical/indirect costs

Cost inputs for pneumococcal disease in included CEAs

- All included CEAs used cost per pneumococcal disease episode for the cost inputs for direct nonmedical/indirect costs
- Parent productivity loss was considered in all CEAs with a societal perspective; three CEAs also considered special education in addition to productivity loss⁴⁻⁶
- Range of cost per episode in the base case is presented in **Figure 3**
 - Compared to direct medical costs, direct nonmedical/indirect costs were generally much lower in pneumococcal disease
 - Similar to direct medical costs, meningitis was associated with the highest cost per episode among all pneumococcal disease types
 - Recurrent/complex AOM and AOM tube placement were also associated with substantial direct nonmedical/indirect costs, comparable to those observed in nonmeningitis invasive pneumococcal disease and inpatient pneumonia

Figure 3. Direct nonmedical and indirect costs per episode of pneumococcal disease^a (2023 USD)



US, United States dollars; AOM, acute otitis media.

^aRanges of base-case cost inputs by disease type and age are presented. Depending on the cost input used in the CEA, it may be included in one or more age categories.

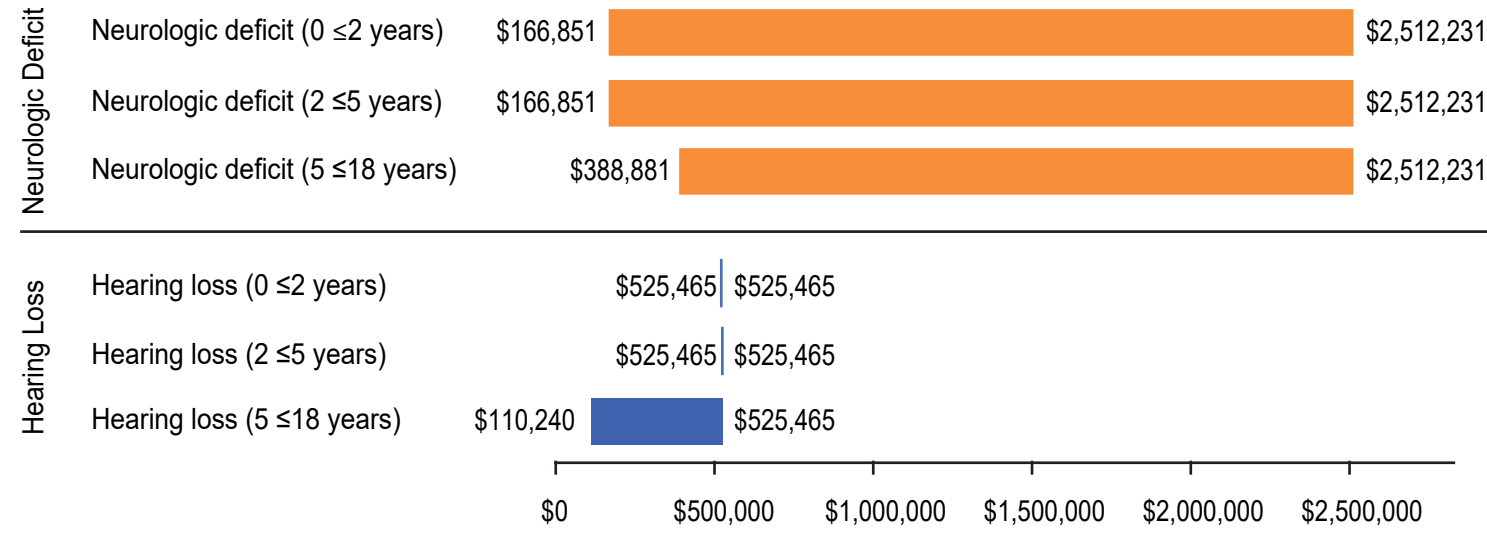
All costs reported in the CEA were converted to 2023 USD using the medical component of the consumer price index.

Direct nonmedical/indirect costs

Cost inputs for post-meningitis sequelae in included CEAs

- Lifetime cost for post-meningitis sequelae was summarized for direct nonmedical/indirect costs since it was used in most CEAs
- Parent productivity loss and special education were considered in all CEAs with a societal perspective
- Range of lifetime costs in the base case is presented in **Figure 4**
 - Contrary to what was observed for pneumococcal disease, lifetime direct nonmedical/indirect costs for post-meningitis sequelae were substantially higher compared to the corresponding direct medical costs
 - Similar to direct medical costs, neurologic deficit was associated with greater direct nonmedical/indirect costs compared to hearing loss

Figure 4. Lifetime direct nonmedical and indirect costs associated with post-meningitis sequelae^a



^aRanges of base-case cost inputs by disease type and age are presented. Depending on the cost input used in the CEA, it may be included in one or more age categories.

All costs reported in the CEA were converted to 2023 USD using the medical component of the consumer price index.

Source data for cost inputs

- Direct medical costs
 - Pneumococcal disease
 - The cost inputs for pneumococcal disease were mostly sourced from unpublished cost analyses that used administrative databases (MarketScan, Kaiser Permanente, and a large New England health plan)
 - Four published cost studies were referenced for the pneumococcal disease cost inputs, which used similar databases (ie, MarketScan and Kaiser Permanente); however, all but one study used data before 2004
 - Overall, costs were much higher from the recently published cost study⁷ compared to those from the unpublished analyses or studies published earlier, even when the same data source was used, e.g.,
 - The range of invasive pneumococcal disease costs was \$48,656 to \$67,855 in the study by Hu T,⁷ while it was \$4,452 to \$25,663 in the unpublished analyses
 - Post-meningitis sequelae
 - The costs inputs for post-meningitis sequelae were all sourced from three published studies using data from 1988 to 1995
 - One published study⁸ was conducted in the Netherlands instead of the US

- Direct nonmedical/indirect costs
 - Pneumococcal disease
 - Unpublished cost analysis based on Kaiser Permanente data was the main source for the direct nonmedical/indirect cost inputs in invasive pneumococcal disease and pneumonia
 - The cost inputs in AOM were sourced from one published study⁹
 - Post-meningitis sequelae
 - The cost inputs for direct nonmedical/indirect costs were sourced from three published studies using data from 1988 to 1997

Conclusions

- Pneumococcal disease and post-meningitis sequelae are associated with high direct medical and direct nonmedical/indirect costs and thus impose substantial economic burdens on the health care system and society
- Substantial variations in cost inputs were observed in the US pediatric CEAs
 - Cost inputs based on a recently published study were generally much higher compared to the ones based on unpublished analyses and those published earlier during the literature review time frame
- These inputs (particularly direct medical costs for post-meningitis sequelae and direct nonmedical/indirect costs for all disease types) were generally sourced to unpublished analyses and data of more than two decades ago, which may substantially underestimate the economic burden of pneumococcal disease and post-meningitis sequelae
- The quality of cost inputs is likely to have a direct impact on the cost-effectiveness of pneumococcal vaccines
- Studies based on more-recent data are indicated to better reflect the economic burden associated with pneumococcal disease and post-meningitis sequelae and provide robust inputs for CEAs of pneumococcal vaccines

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Disclosure

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