# Direct Costs of Pneumococcal Disease in the United States — A Targeted Literature Review

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## Background and objectives

- Pneumococcal disease is a group of conditions caused by *Streptococcus pneumoniae*
- Its clinical presentations include invasive pneumococcal disease (IPD), such as meningitis and bacteremia, and non-invasive diseases, such as non-bacteremic pneumonia (NBP) and acute otitis media (AOM)
- Pneumococcal disease, especially the more serious types, can be expensive to treat and may require prolonged hospitalization
- Estimating the costs of treating pneumococcal disease is important to understand the economic burden of the disease
- It also provides critical inputs for the economic evaluations of pneumococcal vaccines
- The current study aims to synthesize the costs of treating an acute episode of pneumococcal disease in the United States (US) through a targeted literature review

## Methods

### Literature search strategies

- A targeted literature review was conducted in MEDLINE on June 23, 2024, to identify original full-text studies and literature reviews on direct costs of pneumococcal disease published since January 1, 2010
- The references of published reviews were also screened to identify additional original cost studies on pneumococcal disease

### Study selection criteria

*Inclusion criteria*

- Conducted in the US
- Included IPD, pneumonia, or AOM (but did not require these conditions to specifically be caused by *S. pneumoniae*)
- Estimated direct costs per episode for acute pneumococcal disease
- Published in English
- Available as a full-text manuscript

*Exclusion criteria*

- Did not report direct costs for the acute phase
- Costs were incomplete, eg, only including costs for certain procedures or only including inpatient costs for AOM (a condition primarily treated in an outpatient setting)

### Data extraction and evidence synthesis

- The following information was extracted from the original publications
  - Basic study characteristics: Authors, year published, citation
  - Methods: Study design (ie, prospective study, retrospective cohort study or retrospective cross-sectional study), data source, cost estimation methods, and definition of an episode
- Results: Estimated mean or median per-episode costs
- Range of mean costs were summarized by disease type
  - If mean cost was not reported, median cost was used instead
- Median and interquartile range (IQR) of estimated costs per episode from the included studies were estimated
- Costs were converted to 2023 US dollars (USD) using the medical component of consumer price index[1]
- Costs were summarized separately for children (0-17 years) and adults (≥18 years)

## Results

### Overview of included cost studies

- 39 published original cost studies met the selection criteria and were included in the synthesis (**Table 1**)
- 19 and 24 studies were included in the synthesis for children and adults, respectively

**Table 1. Characteristics of included studies**

| Study characteristics | Number of studies |
|---|---|
| Age group | |
| Children | 15 |
| Adults | 20 |
| Both or unspecified age | 4 |
| Disease type in children (0-17 years)[a] | |
| IPD | 8 |
| Pneumonia | 12 |
| AOM | 2 |
| Disease type in adults (≥18 years)[1] | |
| IPD | 7 |
| Pneumonia | 20 |

IPD, invasive pneumococcal disease; AOM, acute otitis media.

[a]The counts included the four studies including both children and adults, in which two focused on IPD only, one focused on pneumonia only, and one included both IPD and pneumonia.

## Children

Summary of methodologies (**Table 2**)

- All included studies were retrospective observational studies, with the majority employing a cohort design (n=16)
- The most common type of data sources was hospital administrative data, which were used to estimate costs of one hospitalization for IPD and inpatient pneumonia
- As a result, more than half of the studies estimated costs using total charges adjusted by cost-to-charge ratios (CCR)
  - One study estimated costs using the total charged amount without applying CCR, resulting in the highest cost estimates
- Definition of one episode varied across studies
  - IPD: Most studies applied one hospitalization to define an episode or a gap of ≥90 days to identify a new episode
  - Pneumonia
    - One hospitalization was most commonly used to define an inpatient pneumonia episode
    - A gap of ≥28 days or 90 days was most commonly used to differentiate two consecutive episodes
  - AOM: In the two included studies, one used a gap of ≥28 days to differentiate two consecutive episodes, while the other used a gap of ≥14 days
- The disease condition also varied across studies for the same pneumococcal disease type, eg:
  - The pneumococcal disease could be caused by different pathogens
  - Studies of IPD focused on meningitis, bacteremia, and sepsis or other IPDs

**Table 2. Summary of methods used in the original cost studies in children**

| | Number of studies | Number of estimates | Study design | | Data source | | | Cost type | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Retrospective cohort study | Retrospective cross-sectional study | Administrative claims data | Hospital administrative data | EMR | Hospital discharge | Hospital discharge adjusted by CCR | Hospital costs | Reimbursement + OOP | Other[a] |
| **Invasive pneumococcal disease** | **8** | **17** | **6** | **2** | **2** | **6** | **0** | **1** | **4** | **1** | **2** | **0** |
| Meningitis | 4 | 8 | 2 | 2 | 1 | 3 | 0 | 1 | 1 | 1 | 1 | 0 |
| Non-meningitis | 5 | 7 | 4 | 1 | 1 | 4 | 0 | 0 | 4 | 0 | 1 | 0 |
| IPD, unspecified | 2 | 2 | 2 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 2 | 0 |
| **Pneumonia** | **12** | **26** | **11** | **1** | **3** | **8** | **1** | **0** | **6** | **0** | **3** | **3** |
| Inpatient pneumonia | 11 | 14 | 10 | 1 | 2 | 8 | 1 | 0 | 6 | 0 | 2 | 3 |
| Outpatient pneumonia | 3 | 4 | 3 | 0 | 2 | 1 | 0 | 0 | 1 | 0 | 2 | 0 |
| Pneumonia, unspecified setting | 4 | 8 | 4 | 0 | 3 | 1 | 0 | 0 | 1 | 0 | 3 | 0 |
| **AOM** | **2** | **9** | **2** | **0** | **2** | **0** | **0** | **0** | **0** | **0** | **2** | **0** |
| Simple AOM/ AOM | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Recurrent/ complex AOM | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| AOM, surgical procedures | 1 | 2 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| AOM, unspecified | 2 | 5 | 2 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 2 | 0 |
| **Total** | **19** | **52** | **16** | **3** | **4** | **14** | **1** | **1** | **10** | **1** | **4** | **3** |

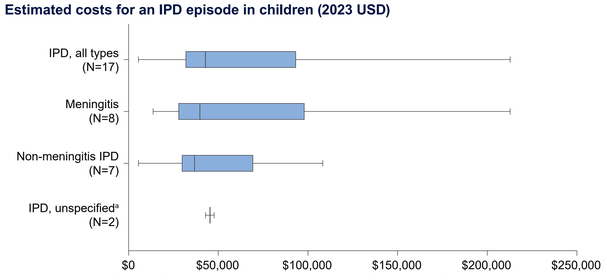
IPD, invasive pneumococcal disease; AOM, acute otitis media; EMR, electronic medical record; CCR, cost-to-charge ratio; OOP, out-of-pocket.

[a]Other cost types included using the resource utilization multiplied by unit costs defined in the study, either developed specifically for the database or obtained from an external data source.

Summary of estimated costs

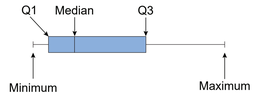
- IPD (**Figure 1A**)
  - There was considerable variability in cost per IPD episode, ranging from $5,462 for an episode of other IPD (ie, neither meningitis nor bacteremia) based on an administrative claims data analysis, to $212,775, which was estimated as total charged amount for one episode of "bacterial meningitis with systemic or focal infections" using a hospital administrative database
  - The median (IQR) costs for an IPD episode was $42,921 ($32,001, $93,156), regardless of the IPD type
- The highest estimate was for unspecified IPD, with a median cost of $45,325 per episode (based on only two estimates)
- The cost was numerically higher for meningitis compared to non-meningitis IPD, with median (IQR) costs of $39,769 ($27,921, $97,954) and $36,766 ($29,889, $69,277), respectively

**Figure 1A. Estimated costs for an IPD episode in children (2023 USD)**




IPD, invasive pneumococcal disease; USD, United States dollar; MIN, minimum; MAX, maximum; Q1, quartile 1; Q3, quartile 3.

The box represents IQR (ie, Q1-Q3), the vertical bar in the box represents the median value; the error bars represent the minimum and maximum values of the cost estimates in the literature.

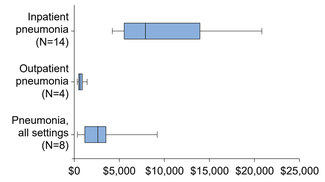



[a]Only median, minimum, and maximum costs were presented in the graph due to limited data points (n=2).

Summary of estimated costs

- Pneumonia (**Figure 1B**)
  - The median (IQR) costs were $7,905 ($5,537, $13,953) for an inpatient pneumonia episode, $621 ($491, $881) for an outpatient pneumonia episode, $2,619 ($1,164, $3,511) for an episode of pneumonia across settings (ie, inpatient and outpatient combined)
  - There was considerable variability in cost estimates for pneumonia, but less so than for IPD
    - Cost for an inpatient pneumonia episode ranged from $4,226 (median cost for an episode of 28 days based on a hospital administrative database) to $20,826 (mean cost for an episode defined using a 90-day gap in an administrative claims database analysis)
  - Two studies evaluated costs for different age groups but did not show consistent trends in costs with increasing ages

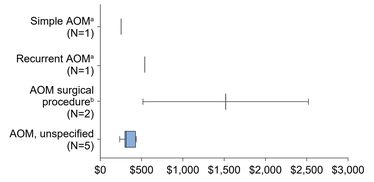
**Figure 1B. Estimated costs for a pneumonia episode in children (2023 USD)**




USD, United States dollar; MIN, minimum; MAX, maximum; Q1, quartile 1; Q3, quartile 3.

The box represents IQR (ie, Q1-Q3), the vertical bar in the box represents the median value; the error bars represent the minimum and maximum values of the cost estimates in the literature.

**Figure 1C. Estimated costs for an AOM episode in children (2023 USD)**




AOM, acute otitis media; USD, United States dollar; MIN, minimum; MAX, maximum; Q1, quartile 1; Q3, quartile 3.

The box represents IQR (ie, Q1-Q3), the vertical bar in the box represents the median value; the error bars represent the minimum and maximum values of the cost estimates in the literature.

[a]Only median cost was presented in the graph as there was only one data point.

[b]Only median, minimum and maximum costs were presented in the graph due to limited data points (n=2).

Summary of estimated costs

- AOM (**Figure 1C**)
  - Most estimates focused on one episode of AOM with unspecified type, with the median (IQR) being $313 ($235, $434)
  - Only one study estimated different types of AOM, showing that AOM surgical procedure had the highest cost (median: $1,512), followed by recurrent AOM (median: $537) and simple AOM (median: $249)
  - One study showed costs decreased with increasing age

## Adults

Summary of methodologies (**Table 3**)

- Similar to the studies in children, all included studies in adults were retrospective observational studies, with the majority employing a cohort design (n=17)
- The most common types of data sources were administrative claims data and hospital administrative data
- Eleven studies estimated costs based on reimbursed amount and patient out-of-pocket costs, while nine studies used hospital costs estimated directly or by applying CCRs. The rest applied unit costs to resource use.
- Definitions of one episode also varied substantially across the studies in adults
  - IPD and pneumonia: One episode was most frequently defined as one hospitalization or using a gap of ≥90 days between two episodes
- The disease condition also varied across studies, particularly for IPD

**Table 3. Summary of methods used in the original cost studies in adults**

| | Number of studies | Number of estimates | Study design | | Data source | | | | Cost type | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Retrospective cohort study | Retrospective cross-sectional study | Administrative claims data | Hospital administrative data | EMR | Other[a] | Hospital discharge adjusted by CCR | Hospital costs | Reimbursement + OOP | Other[b] |
| **Invasive pneumococcal disease** | **7** | **10** | **6** | **1** | **3** | **4** | **0** | **0** | **2** | **2** | **3** | **0** |
| Meningitis | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Non-meningitis | 2 | 3 | 2 | 0 | | 2 | 0 | 0 | 1 | 1 | 0 | 0 |
| IPD, unspecified | 4 | 6 | 4 | 1 | 3 | 2 | 0 | 0 | 1 | 1 | 3 | 0 |
| **Pneumonia** | **20** | **43** | **17** | **3** | **10** | **5** | **3** | **2** | **2** | **4** | **11** | **3** |
| Inpatient pneumonia | 18 | 22 | 15 | 3 | 9 | 5 | 2 | 2 | 2 | 4 | 10 | 2 |
| Outpatient pneumonia | 5 | 9 | 6 | 0 | 5 | 0 | 0 | 1 | 0 | 1 | 5 | 0 |
| Pneumonia, unspecified setting | 6 | 12 | 6 | 0 | 4 | 0 | 1 | 1 | 0 | 1 | 4 | 1 |
| **Total** | **24** | **53** | **17** | **4** | **9** | **7** | **3** | **2** | **4** | **5** | **11** | **3** |

IPD, invasive pneumococcal disease; EMR, electronic medical record; CCR, cost-to-charge ratio; OOP, out-of-pocket.

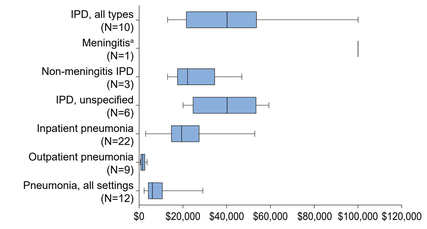
[a]Other databases included linked databases of different types, eg, linked hospital administrative data with claims data or EMR data.

[b]Other cost types included using the resource utilization multiplied by unit costs defined in the study or cost types unspecified.

Summary of estimated costs (**Figure 2**)

- IPD
  - There was considerable variability in cost estimates for an episode of IPD in adults, but was less so than for children, especially within each IPD type
  - The median (IQR) cost for an IPD episode was $40,182 ($21,575, $53,608), regardless of the IPD type
  - The highest cost was for meningitis, with a median per-episode cost of $100,044 estimated using administrative claims data (based on only a single study)
  - The cost was numerically higher for non-meningitis IPD compared to unspecified IPD, with median (IQR) costs of $22,113 ($17,546, $34,510) and $40,182 ($24,651, $53,369), respectively
- Pneumonia
  - The median (IQR) costs were $19,421 ($14,745, $27,407) for an inpatient pneumonia episode, $1,595 ($792, $2,586) for an outpatient pneumonia episode, $6,054 ($4,168, $10,559) for episode of pneumonia across settings
  - There was a wide range of cost estimates for pneumonia, particularly for inpatient pneumonia, ranging from $2,968, estimated for one hospitalization among low-risk patients, to $20,879 for one hospitalization in all inpatients
  - Similar to the studies in children, there was no consistent trend in costs across age groups in adults

**Figure 2. Estimated costs for an episode of pneumococcal disease in adults (2023 USD)**




IPD, invasive pneumococcal disease; USD, United States dollar; MIN, minimum; MAX, maximum; Q1, quartile 1; Q3, quartile 3.

The box represents IQR (ie, Q1-Q3), the vertical bar in the box represents the median value; the error bars represent the minimum and maximum values of the cost estimates in the literature.

[a]Only median cost was presented in the graph, as there was only one data point.

## Summary of findings

- Costs for managing an acute episode of pneumococcal disease were highest for IPD, followed by inpatient pneumonia
- Costs for different types of IPD were overall similar, with evidence suggesting non-meningitis IPD may be associated with lower costs compared to other types
- Costs per episode of IPD were similar between children and adults, but costs for pneumonia were generally higher in adults
- Cost estimates varied widely across studies for each type of pneumococcal disease, reflecting substantial variability in methodologies (eg, disease conditions considered, cost estimation methods, episode definitions)

## Limitations

- The study included both reported mean costs and median costs. However, median costs were generally much lower than mean costs. For the purpose of economic evaluations, mean costs should be used
- The study was unable to summarize costs by age group among children and adults due to limited data in the literature

## Conclusions

- Pneumococcal disease imposes substantial economic burdens on the healthcare system in the US
  - IPD and inpatient pneumonia, in particular, result in considerable costs during the acute phase
- Costs for pneumonia are overall higher in adults compared to children
- Considerable variability in estimated costs across studies highlights the importance of evaluating the methodologies of cost studies when used in economic evaluations
  - Health state definitions and perspectives of the original cost studies should align with those applied in economic evaluations
- There are substantial gaps in cost studies for different types of AOM in children and meningitis in adults

### References

1. US Bureau of Labor Statistics (BLS). Consumer price index for all urban consumers (CPI-U). 2023. https://data.bls.gov/pdq/SurveyOutputServlet. Accessed December 20, 2024.

### Disclosures

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