

Economic Burden of Pneumococcal Disease — Impact of Underlying Medical Conditions

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Background

- Pneumococcal disease is a group of infections caused by *Streptococcus pneumoniae*
- It is associated with high morbidity and mortality, particularly among young children and older adults
- The disease can lead to a substantial economic burden, especially for conditions that require hospitalization
- The presence of underlying medical conditions may increase the risk of developing pneumococcal disease
- In many countries, additional vaccine doses are recommended for individuals with these conditions to prevent pneumococcal disease
- Understanding the impact of these conditions on the costs of pneumococcal disease is essential for assessing the economic value of these additional vaccine doses

Objectives

- To summarize the direct medical costs of an acute episode of pneumococcal disease by risk group or underlying comorbidities, based on a global 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 pneumococcal disease costs published since January 1, 2010
- References cited in published reviews were also screened to identify additional original studies of pneumococcal disease costs

Studies meeting the following criteria were included in this review

- Inclusion criteria
 - Included IPD, pneumonia or acute otitis media (AOM) (but did not require these conditions to specifically be caused by *S. pneumoniae*)
 - Included direct medical costs per episode of acute pneumococcal disease as an outcome
 - Evaluated the impact of risk group or underlying comorbidities on cost per episode, including
 - Reported costs by risk group or individual comorbidities, OR
 - Reported incremental costs associated with a higher risk group or comorbidities
 - Published in English
 - Available as a full-text manuscript
- Exclusion criteria
 - Direct medical costs for an acute episode were not reported (eg, estimates were provided for a 6-month or longer period)

Data extraction and evidence synthesis

- Study characteristics (author and year), pneumococcal disease type, study design, point estimates of direct medical costs per episode by risk group and comorbidities, and incremental costs associated with a higher risk group or comorbidities (if reported) were extracted from included studies
- Median and interquartile range (IQR) of reported mean direct medical costs per episode were estimated by risk group or presence of underlying comorbidities
 - If mean costs were not reported, median costs were used instead
- The relative increase in mean or median direct costs was estimated by comparing groups with a higher risk or comorbidities to those with low risk or no comorbidities in each study
- All costs were converted to 2024 US dollars (USD) using gross domestic product (GDP) deflator in each country and 2024 official exchange rates^{1,2}
- Results were summarized separately for children (0–17 years) and adults (≥18 years)

Results

Overview of included studies (Table 1)

- 22 original cost studies published from 2012 to 2024 met the selection criteria and were included in this review
- 18 studies were conducted in adults; 3 in children; 1 in both age groups
- Pneumonia was included in 20 studies; IPD in 10; none of the studies included AOM
- Half of the studies were conducted in the United States; 9 in European countries; 1 each in Canada and Japan
- 20 were retrospective observational studies; only 2 were prospective studies, including 1 randomized controlled trial

Table 1. Characteristics of studies evaluating costs by risk group or underlying medical conditions

Study characteristics	Number of studies
Age group	
Adults	18
Children	3
Both children and adults	1
Disease type in adults (≥18 years)^a	
IPD	7
Pneumonia	19
Disease type in children (0–17 years)^b	
IPD	3
Pneumonia	2
Study design	
Prospective studies	2
Retrospective observational studies	20
Countries	
US	11
Canada	1
European countries ^c	9
Japan	1

IPD: Invasive pneumococcal disease; US: the United States; UK: the United Kingdom.

^aAll 7 studies on IPD also included pneumonia. ^bOne study included both IPD and pneumonia.

^cOne study was conducted in Belgium, 1 in France, 1 in Germany, 2 in the Netherlands, 2 in Spain, 1 in Sweden, and 1 in the UK.

Risk group/factor definitions (Table 2)

- Of the 22 studies included, 14 explicitly defined risk groups, while the remaining studies evaluated individual comorbidities or a group of comorbidities without implementing risk stratification
- Of the 14 studies defining risk groups
 - 12 classified individuals into the following risk groups based on the presence of comorbidities:
 - High-risk group included individuals with immunosuppressing conditions, such as HIV/AIDS, cancer, and use of immunosuppressants
 - At-risk group consisted of immunocompetent individuals with certain chronic conditions, including chronic cardiovascular, respiratory, and liver diseases, diabetes, smoking, alcoholism, etc.
 - Healthy individuals without the above conditions were generally classified as "low-risk" group
 - 1 defined risk groups based on age and comorbidities
 - 1 defined risk groups using propensity scores
 - 11 studies defined risk groups according to the recommendations of their respective national health authorities
- The remaining 8 studies focused on specific chronic conditions included in these risk groups

Table 2. Definitions of risk groups or risk factors

Definition of risk groups/factors	Sources	Number of studies employing the definition
Risk groups defined based on comorbidities ^a	Recommendations by national health authority	10
	Literature	2
Risk groups defined based on age and comorbidities ^a	Recommendations by national health authority	1
Risk groups defined based on the quintiles from a propensity score for developing pneumonia, incorporating demographics, comorbidities, and treatments	Literature	1
Comorbidities as a group vs no comorbidities	Literature	3
Individual comorbidities vs no comorbidities or overall population	Literature or not specified	5

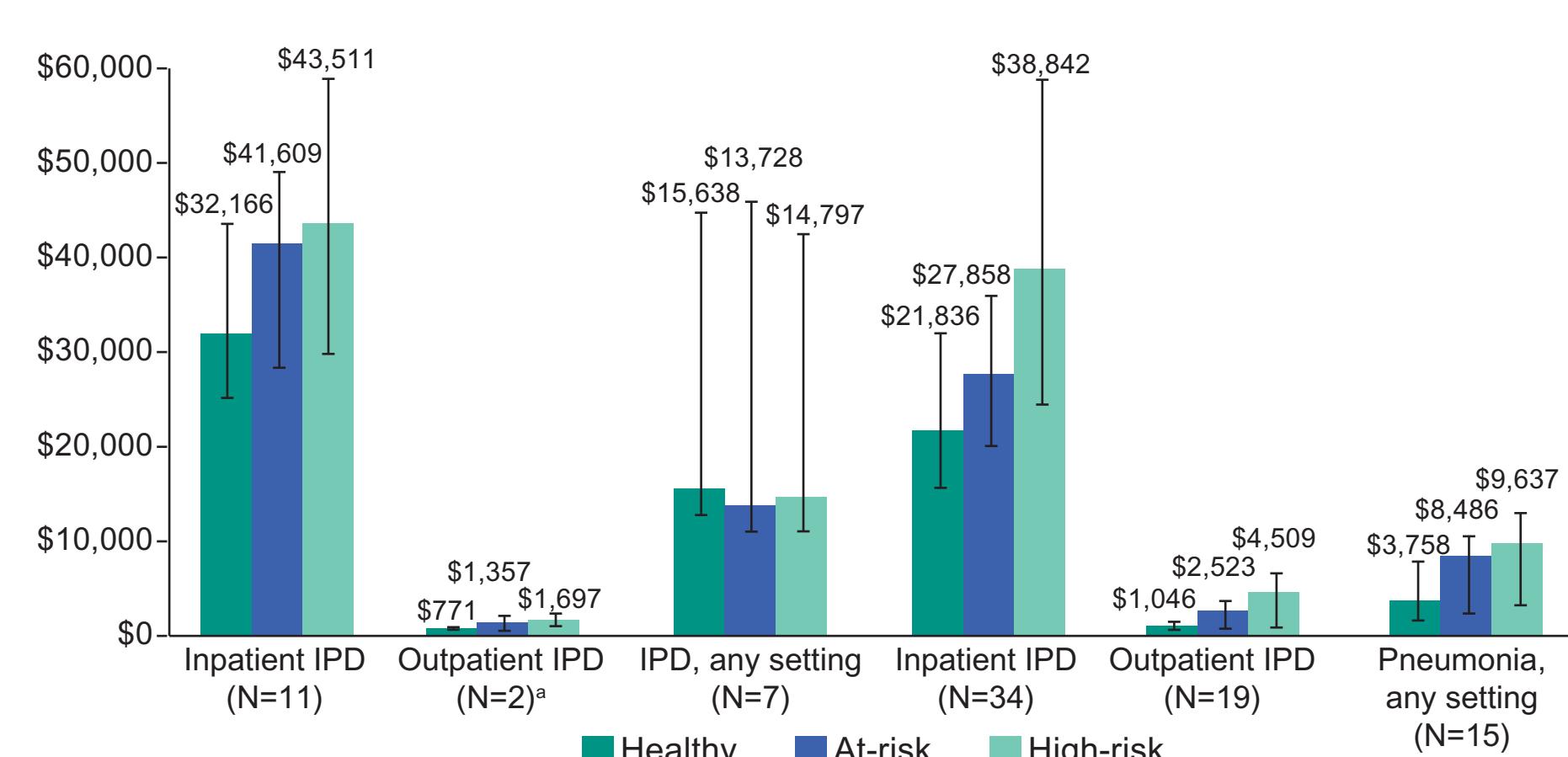
^aThe list of immunocompromising conditions and the list of non-immunocompromising chronic conditions were similar across studies with some variations.

Adults

Summary of direct medical costs by risk group

- 12 studies estimated costs for the three risk groups (healthy, at-risk, and high-risk) in adult populations
 - The median point estimate of direct medical costs increased with risk in all pneumococcal disease categories, except for IPD in any setting (Figure 1)
 - Compared to the healthy group, the median percentage increase in point cost estimate was
 - 11% for inpatient IPD, 87% for outpatient IPD, -7% for IPD in any setting, 16% for inpatient pneumonia, 122% for outpatient pneumonia, and 44% for pneumonia in any setting in the **at-risk group**
 - The corresponding increases in the **high-risk group** were 27%, 113%, -5%, 46%, 256%, and 95%, respectively
 - 8 studies demonstrated a positive trend between mean or median costs and pneumococcal disease risk, while 4 studies reported lower mean costs per episode in individuals with higher risk
 - All 4 studies included both IPD and pneumonia: 3 reported costs for IPD and pneumonia in any setting, while 1 study reported outcomes for all six disease categories
 - All 4 studies reported lower mean costs per episode in individuals with higher risk for IPD; only 1 study showed this trend for pneumonia in any setting
 - Although the percentage increase in mean costs varied across age groups in some studies, no consistent trend was observed

Figure 1. Point estimates of direct medical costs of a pneumococcal disease episode by risk group in adults (2024 USD)



USD: United States dollar; IPD: Invasive pneumococcal disease; IQR: Interquartile range. 12 studies applying the three risk groups (healthy, at-risk, and high-risk) were included. N is the number of data points in each risk group. One study could contribute more than one data point if they reported costs for different age groups in adults.

The bars and numbers shown illustrate estimated medians of the point estimates for each risk group. The error bars represent IQR of the point estimates for each risk group.

^aThere were only two data points in each risk group for outpatient IPD, all from the same study. The error bars indicate range instead of IQR.

- 1 study estimated costs for 5 risk groups defined by age and underlying comorbidities (see definitions in Table 2)
- Compared to adults of 18–64 years without comorbidities, the percentage change in mean cost per episode in higher risk groups were -2%–50% for meningitis, 0%–14% for bacteraemia, 7%–39% for pneumonia in any setting
- Incremental costs in higher-risk groups were primarily driven by age
 - Within the same age group, comorbidities had no or minimal impact on costs (-3%–7% change compared to those without comorbidities)
- 1 study estimated costs for each quintile of probability of developing pneumonia (see definitions in Table 2)
- The study showed a concave relationship between costs per episode and risk, with higher costs observed in the lowest and highest quintiles compared to the other groups

Summary of direct medical costs by comorbidity

- 5 studies compared costs per episode for individuals with vs without specific comorbidities
 - All studies included inpatient pneumonia, and 1 also estimated costs for outpatient pneumonia
 - Most comorbidities were associated with numerically higher costs per episode
 - However, the incremental costs varied by comorbidity and age
 - Liver failure and cancer were associated with lower costs per episode of inpatient pneumonia, possibly due to higher mortality
 - The incremental costs decreased with age

Children

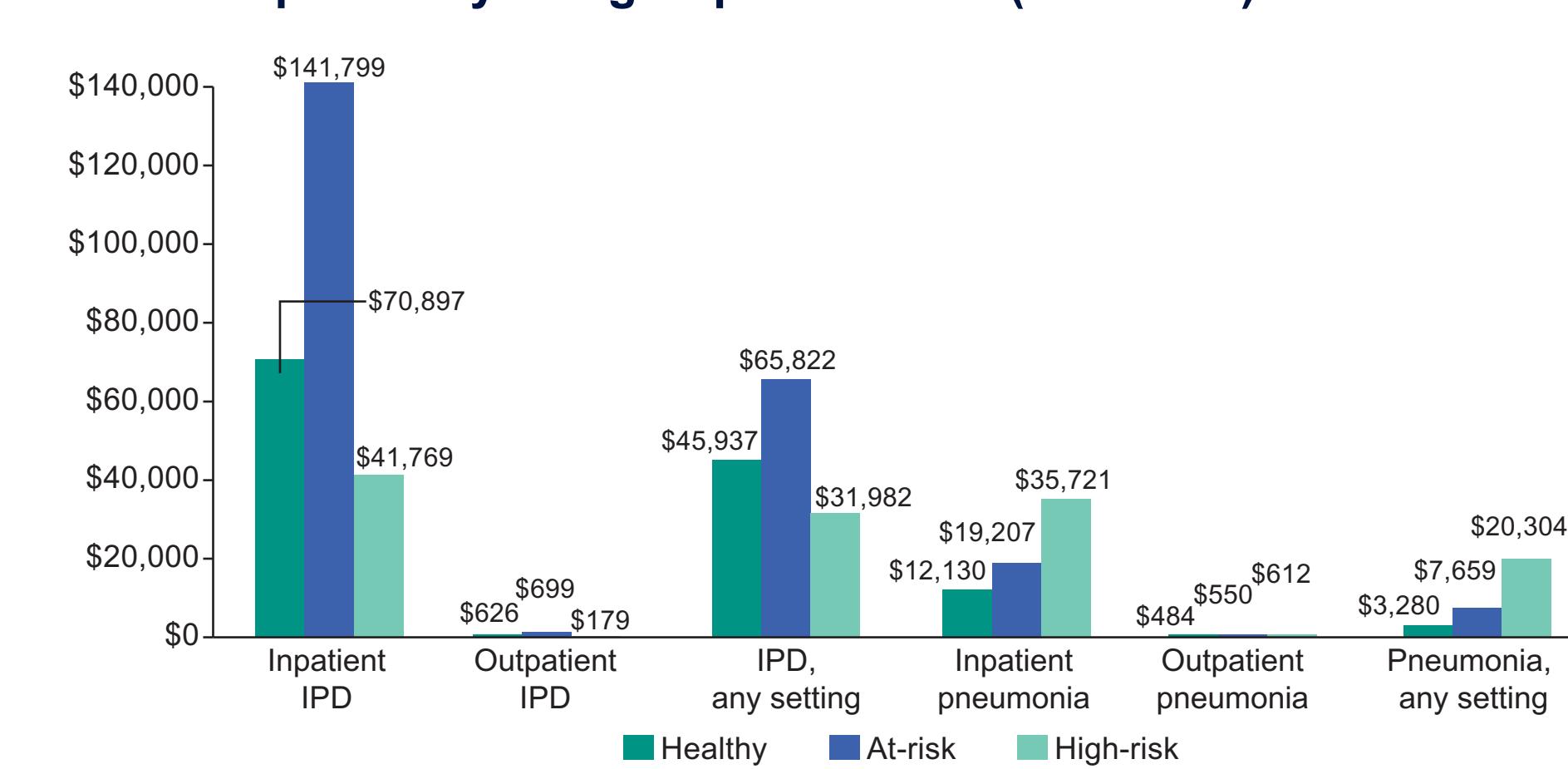
Summary of direct medical costs by risk group

- Only 1 study reported costs per episode by risk group (ie, healthy, at-risk, and high-risk) (Figure 2)
- Costs per episode were highest in the at-risk group and lowest in the high-risk group for all IPD categories, regardless of treatment setting
 - The results may not be reliable due to the small sample sizes in the at-risk and high-risk groups (N<30)
- Costs per episode increased with higher risk for all pneumonia categories

Summary of direct medical costs by comorbidity

- All 3 studies showed that comorbidities were associated with higher costs per episode of pneumococcal disease
 - 1 study showed that the presence of chronic pulmonary disease and other IPD risk factors was associated with 15% higher median cost
 - 1 study reported mean cost per episode increased with the number of comorbidities, ranging from 66%–75% for 1 comorbidity to 295%–384% for 3+ comorbidities
 - Another study reported 17% increase in costs per pneumonia episode for children with acute asthma compared to those without asthma

Figure 2. Point estimates of direct medical costs of a pneumococcal disease episode by risk group in children (2024 USD)



USD: United States dollar; IPD: Invasive pneumococcal disease.

Only one study applying the three risk groups (healthy, at-risk, and high-risk) in children.

The bars and numbers shown illustrate the point estimates for each risk group from that study. Some categories had a small sample size, thus the estimates may not be reliable, including inpatient IPD, outpatient IPD, and IPD (any setting) for the at-risk and high-risk groups (n<30).

Summary of findings

- Definition of risk group/risk factor varied across studies
 - The most common definition was the three risk groups based on comorbidities — high risk (with immunocompromising conditions), at-risk (non-immunocompromising chronic conditions), and healthy (without the specified conditions) — which followed the recommendations of national health authorities
- In adults, costs per episode of pneumococcal disease generally increased with higher risk or presence of comorbidities
 - However, higher risk groups and certain comorbidities (such as liver failure and cancer) were associated with lower costs per IPD episode, possibly due to high mortality among these individuals
- Evidence on the impact of risk group/risk factor in children was limited
 - Existing studies showed that costs per episode increased with higher risk for pneumonia but not for IPD, while comorbidities were associated with higher costs per episode for both IPD and pneumonia
- Overall, substantial variability was observed in how risk and comorbidities affect costs per episode in each pneumococcal disease category, likely due to differences in risk group definitions, included comorbidities, and other aspects of study methodology

Limitations

- The current review focused on costs incurred during the acute episode; long-term costs may also vary by comorbid conditions
- The small number of studies in each pneumococcal disease category prevented further analyses to understand the variability in the outcomes (eg, confounding factors for costs)
- The review did not identify any studies that evaluated the association between costs and comorbidities in AOM

Conclusions

- Risk conditions are generally associated with higher direct medical costs in pneumococcal disease
- The impact of these conditions varies but can be substantial for certain pneumococcal conditions, such as pneumonia in adults
- Preventing pneumococcal disease in populations with a higher risk may reduce the overall economic burden of pneumococcal disease
- There remain significant gaps in understanding the impact of risk conditions on direct costs for pneumococcal diseases, particularly in children

References

- The World Bank Indicators. GDP deflator: linked series (base year varies by country). <https://data.worldbank.org/indicator/NY.GDP.DEFL.ZS>.
- The World Bank Indicators. Official Exchange Rate (LCU per US\$, period average). <https://data.worldbank.org/indicator/PA.NUS.FCRF>.

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