EE551

Indirect Costs Associated With Pneumococcal Disease – A Global Targeted Literature Review

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Background

- Pneumococcal disease is a group of conditions caused by *Streptococcus pneumoniae*, including invasive pneumococcal disease (IPD) (e.g., meningitis and bacteraemia) and non-invasive diseases (e.g., non-bacteraemic pneumonia [NBP] and acute otitis media [AOM])
- These conditions pose a substantial economic burden, including both direct medical costs and indirect costs
- Indirect costs from productivity loss can be significant but are often neglected in cost studies of pneumococcal disease
- Indirect costs are important not only for accurately evaluating the burden of illness related to pneumococcal disease but also in economic evaluations with a societal perspective

Objectives

- To synthesize the indirect costs associated with an acute episode of pneumococcal disease through 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 costs of pneumococcal disease published since January 1, 2010
  - The references of published reviews were also screened to identify additional original cost studies of pneumococcal disease
- Studies on indirect costs were selected based on the following criteria
  - Inclusion criteria
    - Included IPD, pneumonia or AOM (but did not require these conditions to specifically be caused by *S. pneumoniae*)
    - Estimated indirect costs per episode for acute pneumococcal disease
    - Productivity loss was estimated using empirical data
    - Published in English
    - Available as a full-text manuscript
  - Exclusion criteria
    - Productivity loss was obtained from published literature
    - Indirect costs for an acute episode were not reported (e.g., estimates were provided for a 6-month or longer period)
- Data extraction and evidence synthesis
  - The following information was extracted from the original publications
    - Basic study characteristics: authors, year published, citation
    - Methods: study design (i.e., prospective study, retrospective cohort study or retrospective cross-sectional study), data source, cost estimation methods (i.e., human capital approach [HCA] or friction cost approach [FCA]), and definition of an episode
    - Results: estimated mean indirect costs per episode
  - Range of mean costs were summarized by disease type
  - Median and interquartile range (IQR) of estimated indirect costs per episode from the included studies were estimated
  - Costs were converted to 2024 US dollars (USD) using gross domestic product (GDP) deflator in each country and 2024 official exchange rates[1,2]
  - Costs were summarized separately for children (0-17 years) and adults (≥18 years)

Results

Overview of included studies (Table 1 and Table 2)

- 12 original cost studies published from 2010 to 2022 met the selection criteria and were included in the synthesis
- 8 studies were conducted in children and 4 in adults
- All studies were conducted in European countries; studies in other geographic regions were not identified
- Of the 8 studies in children, 1 focused on IPD, 2 on pneumonia, and the remaining 5 on AOM
- All 4 studies in adults focused on pneumonia

Table 1. Characteristics of included studies

Study characteristics	Number of studies
Children (0-17 years)	**8**
IPD	1
Pneumonia	2
AOM	5
Adults (≥18 years)	**4**
IPD	0
Pneumonia	4

IPD: Invasive pneumococcal disease; AOM: Acute otitis media.

Table 2. Summary of studies reporting indirect costs

Author	Year	Country/ region	Pneumococcal disease type	Study type	Data source	Type of indirect costs	Costing approach	Episode definition
Children								
Azzari C	2015	Italy	IPD	Prospective observational study	Health economics data collected for the study	Not specified, likely productivity loss from absenteeism	HCA	One hospitalization (implied)
Keitel	2014	Switzerland	Pneumonia	Prospective observational study	Parental report	Productivity loss from absenteeism	HCA	Episodes separated by ≥30-day of symptom-free period
Lorgelly PK	2010	UK	Pneumonia	Prospective (RCT)	Caregiver telephone interviews	Productivity loss from absenteeism	HCA	Disease onset to parent-reported "back to normal" state for the children
van Uum RT	2021	Netherlands	AOM	Prospective (RCT)	Caregiver diaries and EMR	Productivity loss from absenteeism, presenteeism and unpaid work	HCA	The period from the GP-confirmed diagnosis of AOM to the resolution of symptoms, captured during a 28-day follow-up
Hay AD	2019	England and Wales	AOM	Prospective (RCT)	Caregiver survey	Productivity loss from absenteeism	HCA	8-day after diagnosis
Speets AM	2011a	Portugal	AOM	Retrospective cross-sectional study	Parent survey	Productivity loss from absenteeism, presenteeism, unpaid work, and loss of leisure time	HCA	Most recent episode during the past 12 months
Speets AM	2011b	Sweden	AOM	Retrospective cross-sectional study	Parent survey	Productivity loss from absenteeism, presenteeism, unpaid work, and loss of leisure time	HCA	Most recent episode during the past 12 months
Wolleswinkel-van den Bosch JH	2010	7 European countries	AOM	Retrospective cross-sectional study	Caregiver survey	Productivity loss from absenteeism, presenteeism, unpaid work, and loss of leisure time	HCA	Most recent episode during the past 12 months
Adults								
Rejas J	2022	Spain	Pneumonia	Retrospective multicenter cohort study	EMR	Productivity loss from absenteeism	HCA	Episodes separated by ≥30 days without a CAP diagnosis
Personne V	2016	France	Pneumonia	Prospective observational study	Patient survey	Productivity loss from absenteeism	HCA	Not specified
Cupurdija V	2015	Serbia	Pneumonia	Prospective observational study	Hospital data	Productivity loss from absenteeism	HCA	One hospitalization
Tichopad A	2013	Czech Republic Slovakia Poland Hungary	Pneumonia	Retrospective cross-sectional study	CZ, SK and PL: mandatory national epidemiology reports collected by governmental organizations + retrospective chart review HU: Claims data from the National Health Insurance Fund	Productivity loss from absenteeism	HCA	Not clearly defined (All-cause pneumonia cases were identified based on ICD-10 diagnosis codes)

IPD: Invasive pneumococcal disease; HCA: Human capital approach; UK: United Kingdom; RCT: Randomized controlled trial; AOM: Acute otitis media; EMR: Electronic medical record; GP: General practitioner; CAP: Community acquired pneumonia; CZ: Czech Republic; SK: Slovakia; PL: Poland; HU: Hungary; ICD-10: International Classification of Diseases, 10th Revision.

Children

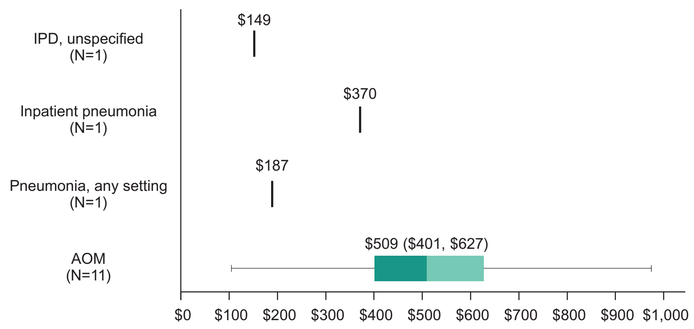
Summary of methodologies (**Table 2**)

- Study type
  - 5 were prospective studies (2 observational studies and 3 randomized controlled trials)
  - 3 were retrospective cross-sectional studies
- Data source
  - Productivity loss data were based on responses from parents or caregivers, collected from survey, telephone interview, or diaries
- Indirect costs components incurred by caregivers were estimated
  - 3 studies included absenteeism only
  - 5 included other components, such as presenteeism, unpaid work, and loss of leisure time
- All studies used HCA to calculate indirect costs by multiplying wage by productivity loss days
- Definition of one episode varied across studies
  - IPD
    - One episode was defined as one hospitalization
  - Pneumonia
    - One study defined the episode from disease onset to "back to normal" state
    - The other study defined the episode using a gap of ≥28 symptom-free days
  - AOM:
    - One episode varied from an 8-day to 28-day period
    - Three studies did not clearly define the episode

Summary of estimated indirect costs incurred by caregivers (**Figure 1**)

- IPD
  - Only 1 study estimated indirect costs for IPD, at $149 per episode
  - The study considered parents' absenteeism during hospitalization only
- Pneumonia
  - One study estimated indirect costs for inpatient pneumonia at $370 per episode, and another estimated indirect costs for pneumonia in any setting at $187 per episode
  - Similar to IPD, these studies only accounted for absenteeism
- AOM
  - Median (IQR) of mean indirect costs for AOM was $509 ($401, $627) per episode, ranging from $105 to $974
  - All studies accounted for absenteeism, presenteeism, and unpaid work, except one study
  - Estimates varied substantially across countries, from $380 to $974 in a multicountry study
  - Indirect costs components and episode duration also seemed to affect the estimates
    - In the UK, one study estimated the mean cost of $105 per episode based on an 8-day duration and absenteeism only, while another study estimated $974 per episode without defining the time frame and included presenteeism, unpaid work, and loss of leisure time, in addition to absenteeism
  - Estimates might also vary depending on how productivity loss was assessed; however, it could not be quantitatively evaluated because limited information was available on the questionnaires used

Figure 1. Mean indirect costs of one pneumococcal disease episode in children (2024 USD)



USD: United States dollar; IPD: Invasive pneumococcal disease; AOM: Acute otitis media; IQR: Interquartile range; Q1=quartile 1; Q3=quartile 3.
Notes: The numbers shown reported median (IQR). The box represents IQR (i.e., 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.
There was only one data point for IPD, inpatient pneumonia and pneumonia (any setting).

Adults

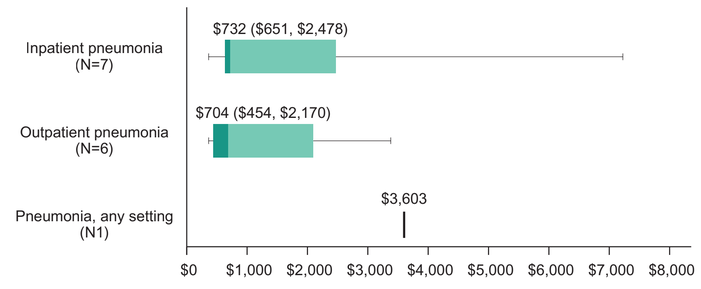
Summary of methodologies (**Table 2**)

- Study type
  - 2 were prospective observational studies
  - 2 were retrospective observational studies (1 cohort and 1 cross-sectional)
- Data source
  - The studies mostly relied on existing databases, including electronic medical records, hospital data, national registers, and claims data
  - 1 study supplemented existing databases with chart review
  - 1 study used patient survey
- Indirect costs components
  - All studies accounted for productivity loss due to absenteeism among patients of working age
- Similar to the studies in children, all 4 studies used HCA to estimate indirect costs
- Episode definition
  - 1 study defined separate episodes using a gap of ≥30 days between two consecutive pneumonia diagnoses
  - 1 study defined the episode as one hospitalization
  - 2 did not provide a clear definition

Summary of estimated indirect costs incurred by patients (**Figure 2**)

- Median (IQR) of point estimates of indirect costs
  - Inpatient pneumonia: $732 ($651, $2,478) per episode
  - Outpatient pneumonia: $704 ($454, $2,107) per episode
  - Pneumonia in any setting: Only 1 study estimated the mean cost at $3,603 per episode
- Indirect costs varied by treatment setting
  - The differences between inpatient and outpatient pneumonia ranged from $−169 to $4,679
  - Most studies showed higher indirect costs for inpatient pneumonia compared to outpatient pneumonia
- Indirect costs varied across countries
  - Based on a multicountry study, the range was $377 to $738 for inpatient pneumonia and $377 to $813 for outpatient pneumonia
- Indirect costs varied by episode definition
  - Episodes defined based on one hospitalization resulted in fewer sick days compared to episodes that included follow-up visits after hospital discharge
- Indirect costs might also vary depending on the data sources for productivity loss and age group

Figure 2. Point estimates of indirect costs of a pneumococcal disease episode in adults (2024 USD)



USD: United States dollar; IPD: Invasive pneumococcal disease; AOM: Acute otitis media; IQR: Interquartile range;
Notes: The numbers shown reported median (IQR).
There was only one data point for pneumonia (any setting).

Summary of findings

- Indirect costs of pneumococcal disease were often estimated based on productivity loss of caregivers for pediatric patients and working-age patients in adult population
- AOM in children is associated with substantial indirect costs
- Indirect costs of pneumonia are high in adults, regardless of treatment settings, though inpatient pneumonia generally incurs higher costs
- Substantial variability exists in indirect costs per episode, likely due to differences in geographic locations, data sources, questionnaires, indirect cost components, and episode definitions

Gaps in literature

- Comprehensive assessment of indirect costs of IPD is lacking for both children and adults
- Evidence on indirect costs of pneumonia in children is limited
- Studies in adults included only working-age patients
  - No studies estimated indirect costs incurred by caregivers for elderly patients
- Most studies on IPD and pneumonia accounted for absenteeism only
  - Indirect costs due to presenteeism, unpaid work, and loss of leisure time can be substantial
- Questionnaires and data sources differed across studies, which may contribute to the substantial variability in estimates of indirect costs
- Most studies did not use validated instruments for productivity loss

Conclusions

- Indirect costs associated with productivity loss for an acute episode of pneumococcal disease can be substantial, particularly for AOM in children and pneumonia in adults
- Considerable variability in estimated indirect costs per episode underscores the need for standardized methodologies to improve the accuracy and comparability of these estimates
- There remain significant gaps in knowledge of the indirect costs associated with pneumococcal diseases in both children and adults

References

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

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