Health Utilities Associated With Pneumococcal Diseases in Children and Adults in the United States — A Targeted Literature Review and Meta-Analysis

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Introduction

- Pneumococcal disease is associated with substantial morbidity and mortality in the United States (US), particularly among young children and older adults[1]
- It can significantly impair health-related quality of life (HRQoL), but these impacts have not been fully evaluated in the US
- HRQoL of pneumococcal disease and its sequelae are not only important to understand the disease burden but also contribute to critical inputs in economic evaluations of new interventions

Objective

- To conduct a meta-analysis of health utilities of pneumococcal disease and post-meningitis sequelae (PMS) in the US

Methods

- This is a subgroup analysis of a global literature review and meta-analysis of health utilities of pneumococcal disease and PMS
- Literature search strategies
  - Two targeted literature searches were conducted in MEDLINE on June 11, 2024, and included original studies and published reviews
    - A review of original studies on health utilities of pneumococcal disease and PMS since 2019
    - A review of cost-utility analyses (CUA) of pneumococcal vaccines since 2010
  - Relevant health utility studies were identified from three sources:
    - References from published literature reviews on HRQoL of pneumococcal disease,[2-4] identified from the literature search in the first review
    - Original health utility studies published since 2019, identified from the literature search in the first review
    - References from published CUAs of pneumococcal vaccines, identified in the second review

Study selection criteria

Inclusion criteria

- Focused on one or more common pneumococcal disease states (ie, meningitis, bacteremia/sepsis, pneumonia, and simple or complex acute otitis media (AOM)) or PMS states (ie, hearing loss, neurological deficits, unspecified PMS)
  - Did not require the condition to specifically be caused by *S. pneumoniae*
- Reported health utility, disutility, quality-adjusted life-year (QALY), or QALY decrement associated with one episode of pneumococcal disease or PMS
- Conducted in the US
- Published in English
- Available as a full-text manuscript

Exclusion criteria

- Focused on a specific population with impaired HRQoL
- Included a condition that differed from pneumococcal or PMS health states
- Estimated the outcomes of pneumococcal disease after an acute episode
- Estimated the outcomes based on assumptions instead of empirical data

Data extraction and preparation

- Utility outcomes were extracted from eligible studies for each pneumococcal disease and PMS health state
- If QALY decrement was not directly reported in the study, the utility outcomes were converted to QALY decrement per episode
- For each category of pneumococcal disease, one estimate per study was included in the meta-analysis using the following methods:
  - Indirect methods (ie, estimating utility values through a generic HRQoL questionnaire) were prioritized over direct methods (eg, time trade-off [TTO] on own health)[5]
  - A weighted average was calculated to combine the estimates from different survey populations or subgroups

Statistical analysis

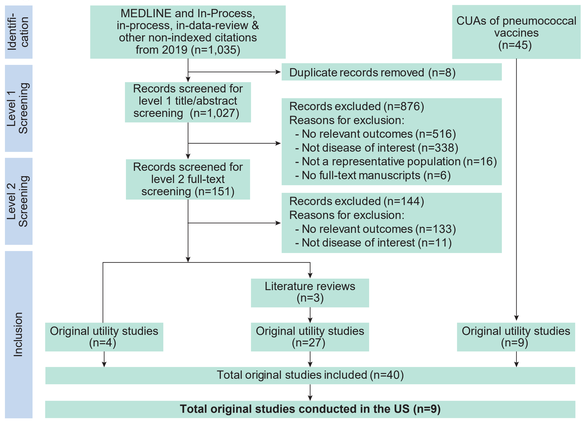
- A meta-analysis was conducted for each category of pneumococcal disease with ≥2 studies
- Pooled estimate of QALY decrement and its 95% confidence interval (CI) were estimated using a random-effects model based on the DerSimonian and Laird method
- Heterogeneity across studies was measured using the between-study variance (τ^2) and the I^2 statistic
- Separate analyses were conducted for children (0-17 years) and adults (≥18 years)

Results

Literature search results

- Nine studies published from 1993-2009 met the selection criteria of the literature review (**Figure 1**)
  - Four studies focused on children only, three on adults only, two on both age groups
  - Studies by age group and disease category are summarized in **Table 1**
- Seven studies were included in the meta-analysis for the following health states (**Table 1**):
  - Children: Meningitis, bacteremia/sepsis, AOM/simple AOM, hearing loss, and neurological deficits
  - Adults: Inpatient pneumonia, outpatient pneumonia, and neurological deficits

Figure 1. PRISMA diagram



PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; CUA, Cost-utility analysis.

Table 1. Summary of identified original health utility studies in the US, by age and disease category

Disease type	Children N	Children References	Adults N	Adults References
IPD				
Meningitis	3	Bennett 2000; IOM 2000; Prosser 2004	1	IOM 2000
Non-meningitis	3	Bennett 2000; IOM 2000; Prosser 2004	1	IOM 2000
Pneumonia				
Inpatient pneumonia	2	IOM 2000; Prosser 2004	2	Coley 1996; IOM 2000
Outpatient pneumonia	2	IOM 2000; Prosser 2004	3	Fryback 1993; Coley 1996; IOM 2000
AOM				
Simple AOM/AOM	3	IOM 2000; Carroll 2009; Prosser 2004	–	NA
Recurrent AOM	1	Prosser 2004	–	NA
Post-meningitis sequelae				
Hearing loss	3	Bennett 2000; Cheng 2000; Carroll 2009	1	Erickson 2001
Neurological deficits	4	Gold 1998; Bennett 2000; IOM 2000; Carroll 2009	2	Gold 1998; IOM 2000
Number of unique studies identified in the literature reviews	**6**		**5**	
Number of unique studies included in the meta-analysis	**5**		**4**	

US, United States; IPD, invasive pneumococcal disease; AOM, acute otitis media; IOM, Institute of Medicine; NA, not applicable. Two studies were excluded from the meta-analysis:

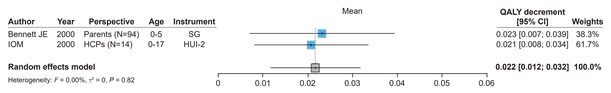
- One study in children (Prosser 2004) was excluded as it was an outlier (due to the methodology)
- One study in adults (Erickson 2001) was excluded because it was the only study that estimated the health utility in the health state (specifically hearing loss)

Health utility of pneumococcal disease in children (0-17 years)

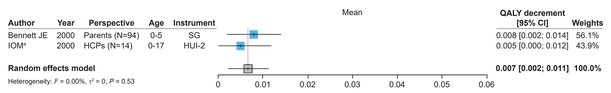
- The included health utility studies employed a variety of methods (**Figure 2** and **Figure 3**)
  - Direct methods: TTO and standard gamble (SG)
  - Indirect methods: Healthy Utilities Index-2 (HUI-2)
  - Other measures: Visual analogue scale (VAS) and Health and Limitations Index (HALex)
- Utility outcomes estimated from the meta-analysis (**Figure 2** and **Figure 3**)
  - Pooled estimates of QALY decrement per episode and their 95% CIs were:
    - IPD: 0.022 (0.012, 0.032) for meningitis and 0.007 (0.002, 0.011) for bacteremia/sepsis
    - AOM/simple AOM: 0.0004 (0.0000, 0.0023)
  - Pooled health utility estimates for PMS and their 95% CIs were 0.829 (0.702, 0.955) for hearing loss and 0.582 (0.386, 0.778) for neurological deficits
- Only one study estimated health utility of pneumonia in children
  - QALY decrements per episode were 0.007 (0.000, 0.019) for inpatient pneumonia and 0.005 (0.000, 0.027) for outpatient pneumonia

Figure 2. Meta-analysis of QALY decrements associated with one episode of pneumococcal disease in children (0-17 years)

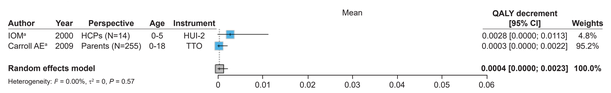
Meningitis



Bacteremia/sepsis



AOM/simple AOM

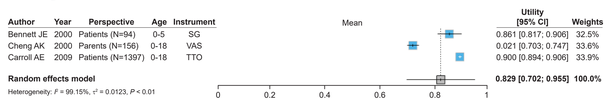


QALY, quality-adjusted life-year; CI, confidence interval; US, United States; AOM, acute otitis media; IOM, Institute of Medicine; HCP, health care professionals; HUI, Health Utilities Index; TTO, time trade-off.

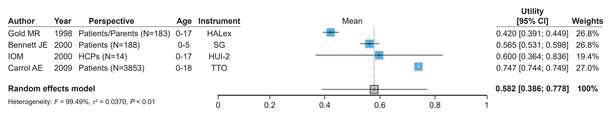
[a]The lower bound of the 95% CI for QALY decrement was truncated at 0.

Figure 3. Meta-analysis of health utility associated with PMS in children (0-17 years)

Hearing loss



Neurological deficits



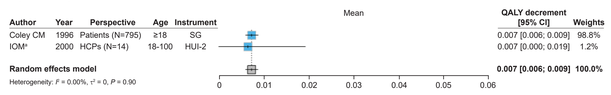
CI, confidence interval; US, United States; IOM, Institute of Medicine; HCP, health care professionals; SG, Standard gamble; VAS, Visual analog scale; TTO, time trade-off; HALex, Health and Limitations Index; HUI, Health Utilities Index.

Health utility of pneumococcal disease in adults (≥18 years)

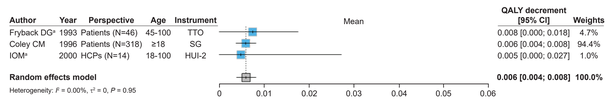
- Similar to the studies in children, the utility estimation methods varied across the studies in adults (**Figure 4** and **Figure 5**)
  - Direct methods: TTO and SG
  - Indirect methods: HUI-2 and EuroQol-5 Dimensions (EQ-5D) index score
  - Other measures: HALex
- Utility outcomes estimated from the meta-analysis (**Figure 4** and **Figure 5**)
  - Pooled estimates of QALY decrement per episode and their 95% CIs were 0.007 (0.006, 0.009) for inpatient pneumonia and 0.006 (0.004, 0.008) for outpatient pneumonia
  - Pooled health utility estimate for neurological deficits and their 95% CIs were 0.470 (0.312, 0.629)
- Only one study was available for IPD and hearing loss, respectively
  - QALY decrements per episode were 0.021 (0.008, 0.034) for meningitis and 0.005 (0.000, 0.012) for bacteremia/sepsis
  - Health utility for hearing loss was 0.730 (based on one observation)

Figure 4. Meta-analysis of QALY decrements associated with one episode of pneumonia in adults (≥18 years)

Inpatient pneumonia



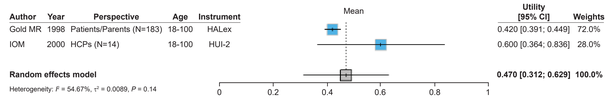
Outpatient pneumonia



QALY, quality-adjusted life-year; CI, confidence interval; US, United States; IOM, Institute of Medicine; HCP, health care professionals; SG, Standard gamble; HUI, Health Utilities Index; TTO, time trade-off.

[a]The lower bound of the 95% CI for QALY decrement was truncated at 0.

Figure 5. Meta-analysis of health utility associated with neurological deficits in adults (≥18 years)



CI, confidence interval; US, United States; IOM, Institute of Medicine; HCP, health care professionals; HALex, Health and Limitations Index; HUI: Health Utilities Index.

Limitations

- Scope of meta-analysis limited due to the limited data available in the literature
  - Unable to conduct the analysis for pneumonia and recurrent AOM in children, as well as IPD and hearing loss in adults
- Substantial heterogeneity in the methodology, reporting, and quality across the included studies
  - Random-effects model accounted for some of this variability
- Certain assumptions necessary to impute missing data when converting health utilities to QALY decrements, which may impact the results
- Subgroup analyses by individual utility estimation method not feasible due to the small number of studies

Conclusions

- Pneumococcal disease and PMS are associated with impaired HRQoL in children and adults in the US, particularly meningitis and neurological deficits
- Existing evidence on health utilities of pneumococcal disease and PMS is limited and may be outdated, as none of the studies were published in the last 15 years
- There was substantial heterogeneity in methods across studies, leading to considerable variability in utility estimates for certain health states, such as neurological deficits in children
- Future studies with more contemporary data and standardized methods are needed to provide more accurate estimates of the impact of pneumococcal disease and PMS on health utility

References

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Disclosures

This study was funded by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (MSD).
MH, EE, and SM are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (MSD).
HR, YS, and DL are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to MSD.
JX is an employee of XL Source, Inc., a consulting company that has provided paid consulting services to this research project.
DR and MSK receive consulting fees from MSD.
DR is a member of the EuroQoL group.

Presented at ISPOR; Montreal, QC, Canada; May 13-16, 2025.