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Assessment of Health State Utilities for Invasive Pneumococcal Disease, Pneumonia, and Acute Otitis Media in Young Children

Louis S. Matza[1], Timothy A. Howell[1], Bianca Chun[2], Lucinda Hetherington[3], Meghan White[2], Thomas Weiss[2], Min Huang[2], Donna Rowen[4], Tina Tan[5], Kristen Feemster[2], Bayad Nozad[6], Matthew Kelly[7], Salini Mohanty[2]

[1]Patient-Centered Research, Evidera, Bethesda, MD, USA; [2]MRL, Merck & Co., Inc., Rahway, NJ, USA; [3]Patient-Centered Research, Evidera, London, UK; [4]Sheffield Centre for Health and Related Research, University of Sheffield, Sheffield, UK; [5]Feinberg School of Medicine, Northwestern University, Chicago, IL, USA; [6]Imperial College London, London, UK; [7]Department of Pediatrics, Duke University School of Medicine, Durham, NC, USA

Background

- *Streptococcus pneumoniae* is a common bacterium with more than 100 identified serotypes.[1] The bacterium can exist harmlessly in the nasopharynx of healthy individuals but can also cause severe disease, particularly in young children.[2,3]
- If *S. pneumoniae* spreads outside of the nasopharynx, it can cause diseases such as acute otitis media (AOM) and pneumonia. If *S. pneumoniae* invades normally sterile sites, including the blood stream or cerebrospinal fluid, it can result in invasive pneumococcal disease, which includes serious infections such as meningitis, bacteremia, and sepsis.[2,3]
- Vaccines are in development to protect against pneumococcal disease in adults and children. Cost-utility analyses will be useful for examining the value of these vaccines, and these models require health state utilities as inputs.
- Published utilities associated with these infections are limited.[4-9]
- The purpose of this vignette-based utility elicitation study was to estimate utilities associated with various infections caused by *S. pneumoniae* so that these utilities may be used in cost-utility models examining the value of vaccines.

Methods

Study Design

- Six health state vignettes were drafted based on published literature and interviews with six clinicians with experience treating children with infections caused by *S. pneumoniae* (see example of a health state in **Figure 1** and a complete list of health states in **Table 1**).
- These health states were valued in time trade-off (TTO) utility interviews conducted in March 2023 with a sample of general population respondents in London and Edinburgh, UK.

Figure 1. Sample Health State

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Infection	• The **child has an infection** caused by a common type of bacteria that is found in the nose and throat but can spread to other parts of the body and cause illness. • In this case, the bacteria have spread into the lungs.
Symptoms	• Symptoms begin as a **typical cold or flu-like infection.** • Over the next few days, the child develops **high fever, fatigue, cough, congestion, difficulty breathing,** and **decreased appetite.** • The child is **not as active** as usual**.**
Treatment and Hospitalisation	• The child is **admitted to hospital** and is put on **intravenous (IV) antibiotics.** ○ This means a needle is inserted into the child's arm and is attached to a tube, through which medication flows into the child. • At times, the child requires **supplemental oxygen**, which is given by a small tube placed under the nose. • Symptoms **begin to improve after about 2-3 days.** At this point, antibiotic **treatment is changed from IV to oral (liquid or tablets)** and the child is **discharged from hospital.** • For some children, these IV and oral antibiotics can have mild side effects (most commonly diarrhoea and upset tummy). • The full course of **antibiotic treatment is 10 days,** including the IV and oral treatment.
Return to School	• The child is able to return to pre-school (or school) once they are feeling better, **about a week after being discharged from hospital.**
Timeline Starting at Hospitalisation	**Day 0** In hospital with IV antibiotics **Day 2 – 3** Symptoms begin to improve, switched to oral antibiotics, leaves hospital **Day 10** End of all antibiotics and return to school

Table 1. Health States

Health State	Infection	Number of Days in Hospital	Number of Days on Antibiotics
Recurrent AOM Health States			
A	Recurrent AOM	0	10 days per episode
B	Recurrent AOM treated with PE tubes	0	10 days per episode
One temporary infection valued in the context of a year			
C	Pneumonia	2-3	10 per year
D	Bacteremia	3-4	10-14 per year
E	Bacteremic Pneumonia	2-3	10 per year
F	Meningitis	10-14	10-14 per year

Participants

- All participants met the following criteria:
  1. >18 years of age
  2. Able to understand the assessment procedures as judged by the investigator
  3. Able and willing to give written informed consent
  4. Able to complete the protocol requirements
  5. UK resident

Pilot Study

- Prior to the main study, a pilot study was conducted to finalize the interview procedures and health state descriptions (N = 28; mean age = 50.8 years; 50% female).
- Participants completed health state valuation tasks and then provided feedback on health states and interview procedures. Almost all participants had no difficulty understanding the health states or the TTO task.
- Three TTO variations were tested in the pilot study: a 1-year time horizon, a 10-year time horizon, and a lag-time approach. Based on feasibility and logic of the responses in this pilot study, the 10-year approach was selected for the main study.

Procedures

- Participants first completed an introductory ranking task. Then, participants valued the health states in a TTO task. After completing the TTO portion of the interview, the participants also completed a demographic and clinical information form.
  - Health state A (recurrent AOM) was valued as a chronic health state, unchanging for the 10-year period (i.e., four infections per year).
  - Health state B (AOM with one pressure equalization [PE] tube procedure) repeated annually, with one PE tube procedure each year.
  - Health states C through F each described a single temporary *S. pneumoniae* infection (hospitalized pneumonia, bacteremia, bacteremic pneumonia, meningitis). Participants were instructed to imagine a 10-year period in which these infections occurred once per year (so results could be used to calculate a quality-adjusted life year [QALY] decrement associated with each infection). Other than these infections, the child lived their life in full health.
- Participants were told to imagine that the hypothetical child experiencing these infections was 2, 3, 4, or 5 years old at the beginning of the time horizon. Assignment to one of these four ages was randomized.
- Health states were ranked and rated in two groups (AOM health states [A, B] and temporary infections [C, D, E, F]). Half of the participants were randomized to rank and rate the AOM health states first (A, B), while the other half was given the other group first (C, D, E, F).

Results

Sample Description

- A total of 208 participants completed the TTO utility elicitation.

Health State Rankings

- Health states A (recurrent AOM) and B (recurrent AOM with PE tube procedure) were ranked together, with health state A preferred by slightly over half of the participants (52.4%).
- Health states C to F were ranked together, with health state C (hospitalized pneumonia) most preferred by approximately two-thirds of participants (66.3%). Health state F (meningitis) was most commonly ranked last (97.6%).

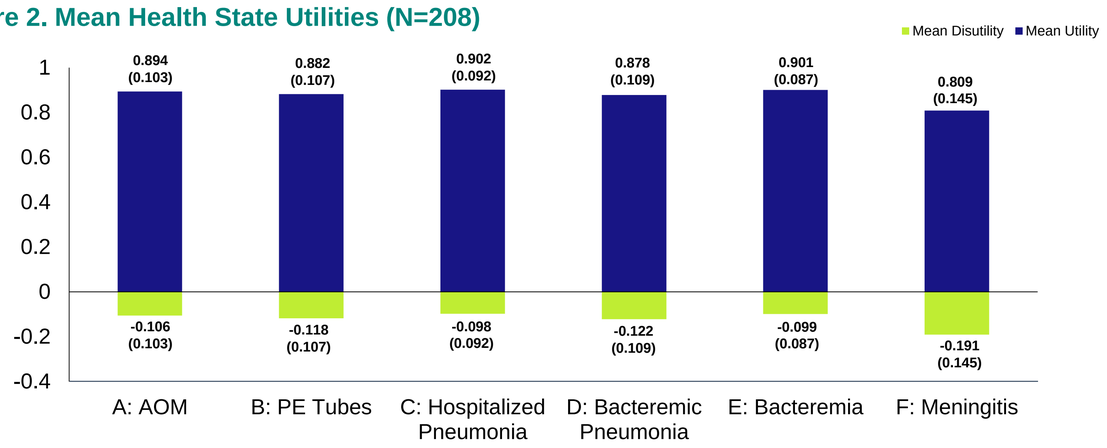
Table 2. Demographic Characteristics

Characteristic	Total Sample (N=208)
Age (Mean, SD) (years)	41.0 (14.9)
Gender, n (%)	
Male	98 (47.1%)
Female	108 (51.9%)
Nonbinary	1 (0.5%)
Prefer not to answer	1 (0.5%)
Ethnicity, n (%)	
Asian/Asian British	20 (9.6%)
Black/African/Caribbean/Black British	5 (2.4%)
White	162 (77.9%)
Mixed/Multiple ethnic groups	12 (5.8%)
Other	9 (4.3%)
Employment Status, n (%)	
Full-time work	98 (47.1%)
Part-time work	52 (25.0%)
Other	58 (27.9%)
Education Level, n (%)	
Less than university degree	55 (26.4%)
University degree or higher	153 (73.6%)
Parent or Guardian of Child, n (%)	
Yes	64 (30.8%)
No	144 (69.2%)
If 'yes' to previous question...Child has had any of the following infections/procedures, n (%; not mutually exclusive)	
Otitis media	46 (34.1%)
Pneumonia	8 (5.9%)
Bacteremia	3 (2.2%)
Meningitis	4 (3.0%)
Ear tubes	6 (4.4%)

Health State Utilities

- Mean (SD) utilities and disutilities (i.e., utility decrease from full health) are in **Figure 2**. See the Conclusions section below for how these values may be interpreted and used in models.
- Mean (SD) disutilities (i.e., decreases from full health) ranged from -0.122 (0.109; bacteremic pneumonia) to -0.098 (0.092; hospitalized pneumonia), except for meningitis, which had a disutility of -0.191 (0.145).

Figure 2. Mean Health State Utilities (N=208)



Limitations

- Limitations of vignette-based methods should be acknowledged. Utilities are derived from general population preferences for hypothetical health state vignettes, rather than the experiences of actual patients. Comparability between the currently reported values and utilities derived from patients is unknown.

Conclusions

- Utilities followed expected patterns. Lower utilities were associated with health states that had longer follow-up/treatment periods, required more invasive treatments/tests, and described infections that were perceived as more severe.
- Results can be interpreted in ways that are useful for subsequent cost-utility models:
  - The utility of health state A can be used for any duration of time in a model to represent children suffering from recurrent AOM.
  - The difference between health states A and B represents the QALY impact of receiving the PE tube procedure.
  - Disutilities of health states C to F (in **Figure 2**) can be considered a QALY decrement that may be applied in a model to represent the impact of each individual infection.
- Results have implications for the assessment of pediatric utilities. Several aspects of the study are unique, including the application of vignette-based methods to health states representing temporary health-related experiences of children as young as 2 years old.
- The utilities estimated in this study may be useful in models examining and comparing cost-effectiveness of various treatments or vaccines for infections caused by *S. Pneumoniae.*

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