Health-related utilities associated with pneumococcal disease in the adult population — what do we know?

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Background

- Cost-effectiveness analysis (CEA) provides important evidence to assess the economic value of new pneumococcal vaccine strategies
- The rigor of CEA relies on robust model inputs, in which health-related utilities constitute a crucial component
- To date, no studies have synthesized the health-related utilities used in the CEAs of pneumococcal disease (PD) in the United States (US)

Objectives

- To summarize health-related utilities associated with PD (such as invasive PD, pneumonia, or post-meningitis sequelae) in adults, based on CEAs of pneumococcal vaccines in the US

Methods

- Literature search strategies
  - A targeted literature review was conducted in 2023 using MEDLINE
  - Original full-text studies and literature reviews, including US CEAs of adult pneumococcal vaccines, published from 2019 were reviewed
  - CEA publications included in the identified literature reviews were screened, and eligible articles identified were also included in this study
- Study selection criteria for CEAs were described in Table 1
- In addition, the original utility studies from which the health utility inputs were obtained were reviewed
- Evidence synthesis
  - Quality of life (QoL)-related model inputs, such as health state utilities or quality-adjusted life-year (QALY) decrements, utilized in the included CEAs were summarized
  - Health state utility inputs were converted to QALY decrements using the reported duration of illness for PD
  - QoL-related utility values reported in the original utility studies and methods used to derive these values were also summarized

Table 1. PICOS criteria for CEA study selection

	Inclusion criteria	Exclusion criteria
Population	Adults in the US	• Children (<18 years old) • Countries other than US
Intervention	Pneumococcal vaccine	Interventions not related to pneumococcal vaccines
Comparator	Any comparator	
Outcomes	QALY	• Only cost outcomes • Effectiveness outcomes other than QALYs
Study design	Cost-utility analysis	• Cost analysis • Cost-benefit analysis • CEA with effectiveness outcomes other than QALYs
Publication year	1990-present	Published before 1990

PICOS, population, intervention, comparator, outcomes, and study design; US, United States; QALY, quality-adjusted life-year; CEA, cost-effectiveness analysis.

Results

Overview of selected CEAs

- Twenty-eight CEA studies met the selection criteria and were included in the synthesis
- Twenty-four CEA studies (86%) referenced other CEA studies for health utility inputs
- All CEA studies ultimately sourced the health utility inputs from 5 original studies
- The number of CEA studies by disease type and health utility measures reported are presented in Table 2
  - For IPD and inpatient pneumonia, the majority of the CEA studies reported health state utilities, which could be converted to QALY decrements based on duration of illness; 5 studies reported directly QALY decrements due to one episode of IPD and/or inpatient pneumonia
  - For outpatient pneumonia, most of the CEA studies reported QALY decrements/disutilities, while 3 studies reported health utilities
  - For disability, all studies reported health utilities

Table 2. Summary of CEA studies by disease type and health utility measures

Disease type	Number of CEAs	Type of health utility reported			Number of original QoL/utility studies referenced
		Utility	QALY decrement	Disutility[a]	
IPD	26	21	5		3
IPD overall	23	19	4		3
Meningitis	1		1		1
Bacteremia	2	2			1
Other IPD symptoms	1		1		1
Pneumonia[b]	21	16	5	8	4
Inpatient pneumonia	20	16	4		4
Outpatient pneumonia	16	3	5	8	2
PMS	18	18			1
Disability	18	18			1

CEA, cost-effectiveness analysis; QALY, quality-adjusted life-year; QoL, quality of life; IPD, invasive pneumococcal disease; PMS, post-meningitis sequelae.
[a]Disutility was reported for outpatient pneumonia in 8 studies; however, they were the same as QALY decrements and thus were combined with QALY decrements in the summary.
[b]The number of studies reporting each type of health utility added up to more than 21 because certain studies reported utilities for inpatient pneumonia but QALY decrements/disutilities for outpatient pneumonia.

Health-related utilities associated with invasive pneumococcal disease (IPD)

- Twenty-six CEA studies reported health-related utilities associated with IPD; 21 studies reported utilities, and 5 studies reported QALY decrements
  - All 21 studies cited a utility of 0.2, which was based on the utility value assumed for hospitalization (Erickson PJ, 1995; Torrance GW, 1995)
  - The QALY decrements applied for one episode of IPD in the five CEAs ranged from 0.0051 to 0.0232 in the base case, which were all sourced from the study by Bennett JE, 2000
- Summary of reported or derived QALY decrements from the CEAs (Figure 1)
  - QALY decrements ranged from 0.003 to 0.8 per episode in the base case for adults without underlying medical conditions in all 26 CEAs; the range was 0.003-0.0745 per episode after excluding the outlier (Ishigami J, 2019)
  - Based on the duration of illness of 34 days reported in 10 studies, a QALY decrement of 0.0745 was estimated for the 20 studies reporting the utility value of 0.2
  - The outlier study (Ishigami J, 2019) assumed that the utility of 0.2 was the yearly average and thus led to the highest QALY decrement of 0.8
  - Five CEAs reported QALY decrements directly based on one utility study (Bennett JE, 2000), which estimated QALYs associated with meningitis and bacteremia in children
    - However, the QALY decrements varied substantially, ranging from 0.006 for overall IPD (Dhankhar P, 2000) to 0.0232 for meningitis (Cho BH, 2013)
      - The lower end corresponded to QALY decrement for local infection, while the higher end corresponded to meningitis with recovery
      - Three studies used a weighted average of bacteremia and meningitis to estimate QALY decrements for IPD (Stoecker C, 2016; Stoecker C, 2020; and Kobayashi M, 2022)
    - The QALY decrement was smaller among patients with comorbid conditions (Cho BH, 2013)

Health-related utilities associated with inpatient pneumonia

- Twenty studies reported utility inputs for inpatient pneumonia
  - Sixteen studies reported utilities
    - Fourteen cited a utility of 0.2, same as for IPD, which was based on the utility value assumed for hospitalization (Erickson PJ, 1995; Torrance GW, 1995)
    - Two derived a utility of 0.85 from a study estimating utilities for various health conditions (Fryback DG, 1993); however, the details of the estimation were not described
  - Four studies applied QALY decrements for one episode of inpatient pneumonia, ranging from 0.0038 to 0.006, based on the study by Bennett JE, 2000
- Summary of reported or derived QALY decrements from the CEAs (Figure 2)
  - QALY decrements ranged from 0.006 to 0.8 per episode in the base case for adults without underlying medical conditions in all 20 CEAs; the range was 0.006-0.0745 per episode after excluding the outlier (Ishigami J, 2019)
  - Based on the duration of illness of 34 days reported in 11 studies, a QALY decrement of 0.0745 was estimated for the 14 studies reporting the utility value of 0.2
  - Based on the disease duration of 4 days of hospitalization followed by 5 and 14 days in outpatient convalescence, the QALY decrements were estimated to be 0.0030 and 0.0056 in the two studies reporting the utility value of 0.85
  - The outlier study (Ishigami J, 2019) assumed that the utility of 0.2 was the yearly average and thus led to the highest QALY decrement of 0.8
  - Four studies reported QALY decrements directly
    - All used the same value of 0.006 for adults without underlying medical conditions from the study by Bennett JE, 2000
    - The QALY decrement ranged from 0.0038 to 0.006 when adults with and without medical conditions were included
    - The QALY decrement was smaller among patients with comorbid conditions (Cho BH, 2013)

Health-related utilities associated with outpatient pneumonia

- Sixteen studies reported utility inputs for outpatient pneumonia
  - Three studies reported utilities
    - One study used the utility of 0.791, also from the study by Bennett JE, 2000
    - Two derived a utility of 0.90 from a study estimating utilities for various health conditions (Fryback DG, 1993); however, the details of the estimation were not described
  - Thirteen studies applied QALY decrements ranging from 0.0026 to 0.004, based on the study by Bennett JE, 2000
- Summary of reported or derived QALY decrement from the CEAs (Figure 3)
  - QALY decrements ranged from 0.0014 to 0.004 per episode in the base case for adults without underlying medical conditions
  - Based on the disease duration of 5 and 14 days in outpatient convalescence, the QALY decrements were estimated to be 0.0014 and 0.0038 in the two studies reporting the utility value of 0.90
  - Based on the duration of illness of 0.019 years, a QALY decrement of 0.004 was estimated for the study reporting a utility value of 0.791, the same as the 13 studies reporting QALY decrements directly
  - Thirteen studies reported QALY decrements directly
    - All used the same value of 0.004 for adults without underlying medical conditions, which was derived from the study by Bennett JE, 2000
    - The QALY decrement ranged from 0.0027 to 0.004 when adults with and without medical conditions were included
    - The QALY decrement was smaller among patients with comorbid conditions (Cho BH, 2013)

Health-related utilities associated with post-meningitis sequelae (PMS)

- Eighteen studies reported a utility of 0.4 (range 0.21-0.59) for disability (Table 3)
- The source study was Gold MR, 1998, which estimated the utilities of various conditions based on the National Health Interview Survey (NHIS) 1987-1992
  - The base case (0.4) corresponded to the mean value for patients with paraplegia
  - The lower limit (0.21) corresponded to the median value for patients with hemiplegia
  - The upper limit (0.59) corresponded to the mean value for patients with cerebral palsy

Table 3. Summary of health utility inputs for disability in the CEA studies

Author and year	Health state in the CEA	Type of utility input	Base-case value	Range	Reference
Smith KJ, 2008	Disability	Utility	0.4	0.2-0.6	Gold MR, 1998
Smith KJ, 2009	Disability	Utility	0.4	0.2-0.6	Gold MR, 1998
Smith KJ, 2010a	Disability	Utility	0.4	0.2-0.6	Gold MR, 1998
Smith KJ, 2010b	Disability	Utility	0.4	0.2-0.6	Gold MR, 1998
Smith KJ, 2012	Disability	Utility	0.4	0.2-0.6	Gold MR, 1998
Smith KJ, 2013a	Disability	Utility	0.4	0.2-0.6	Estimate
Smith KJ, 2013b	Disability	Utility	0.4	0.2-0.6	Gold MR, 1998
Smith KJ, 2021a	Disability	Utility	0.4	0.21-0.59	Gold MR, 1998
Smith KJ, 2021b	Disability	Utility	0.4	0.21-0.59	Gold MR, 1998
Smith KJ, 2022	Disability	Utility	0.4	0.21-0.59	Gold MR, 1998
Ishigami J, 2019	Disability	Utility	0.4	0.21-0.59	Gold MR, 1998
Wateska AR, 2019a	Disability	Utility	0.4	0.21-0.59	Gold MR, 1998
Wateska AR, 2019b	Disability	Utility	0.4	0.21-0.59	Gold MR, 1998
Wateska AR, 2020a	Disability	Utility	0.4	0.21-0.59	Gold MR, 1998
Wateska AR, 2020b	Disability	Utility	0.4	0.21-0.59	Gold MR, 1998
Wateska AR, 2020c	Disability	Utility	0.4	0.21-0.59	Gold MR, 1998
Wateska AR, 2022	Disability	Utility	0.4	0.21-0.59	Gold MR, 1998
Chen D, 2014	Disability (new cases)	Utility	0.400		Smith KJ, 2012
Chen D, 2014	Disability (survivors)	Utility	0.400		Smith KJ, 2012

CEA, cost-effectiveness analysis.

Summary of original utility studies

- The 28 CEAs used utility inputs from 5 original studies dated from 1993 to 2000 (Table 4)
  - Four studies (Fryback DG, 1993; Erickson PJ, 1995; Torrance GW, 1995; and Gold MR, 1998) were not specific to PD
  - Bennett JE, 2000, estimated utilities associated with IPD in children aged 3-36 months
  - None of the original studies estimated utilities for PD in an adult population
- Except for Sisk JE, 1997, none of the CEA studies described how the utility inputs were derived based on the results from these original studies
  - The utility inputs could be matched to the original studies by Erickson PJ, 1995; Torrance GW, 1995; Bennett JE, 2000; and Gold MR, 1998
  - Vold Pepper, 2002, derived the utilities for hospitalization with pneumonia and outpatient pneumonia from the study by Fryback DG, 1993. However, the numbers could not be matched to the results in the original study

Table 4. Summary of the original studies citied for the utility inputs in the CEAs

First author	Published year	Health state in the original QoL/utility study	Utility/QALY value	Range	Health states used in CEAs	Methods
Fryback DG	1993	Chronic bronchitis	0.67 (QWB) 0.724 (TTO)	0.65-0.70 (QWB) 0.657-0.791 (TTO)	Hospitalization with pneumonia Outpatient pneumonia	Survey of patients with chronic conditions using QWB and TTO in the Beaver Dam Eye Study
Erickson PJ	1995	Fair health and limited in instrumental activities of daily living (IADL)	0.21		IPD Hospitalization Hospitalized nonbacteremic pneumonia	Assumptions made on assigned utility to different levels of self-rated health status and activity limitations
Torrance GW	1995	Limited in IADL	0.20		IPD	Assumptions made on assigned utility values to different levels of activity limitations
Gold MR	1998	Paraplegia Hemiplegia Cerebral palsy	0.4	0.21-0.59	Disability after IPD	Health-related quality of care weights were derived based on self-rated health status and activity limitations in the NHIS 1987-1992 survey
Bennett JE	2000	Meningitis with recovery	0.9768	0.5970-1.0000	Meningitis IPD	Interview of parents with children aged 3-36 months presenting in an urban children's hospital. Standard gamble was used to derive utilities for different scenarios describing the outcomes of occult bacteremia. The results were used in CEA studies as QALYs
		Hospitalization in occult bacteremia	0.9921	0.7825-1.0000	Other IPD syndrome IPD	
		Local infection in occult bacteremia	0.9941	0.7948-1.0000	Hospitalization Outpatient pneumonia	

Figure 1. QALY decrements associated with IPD

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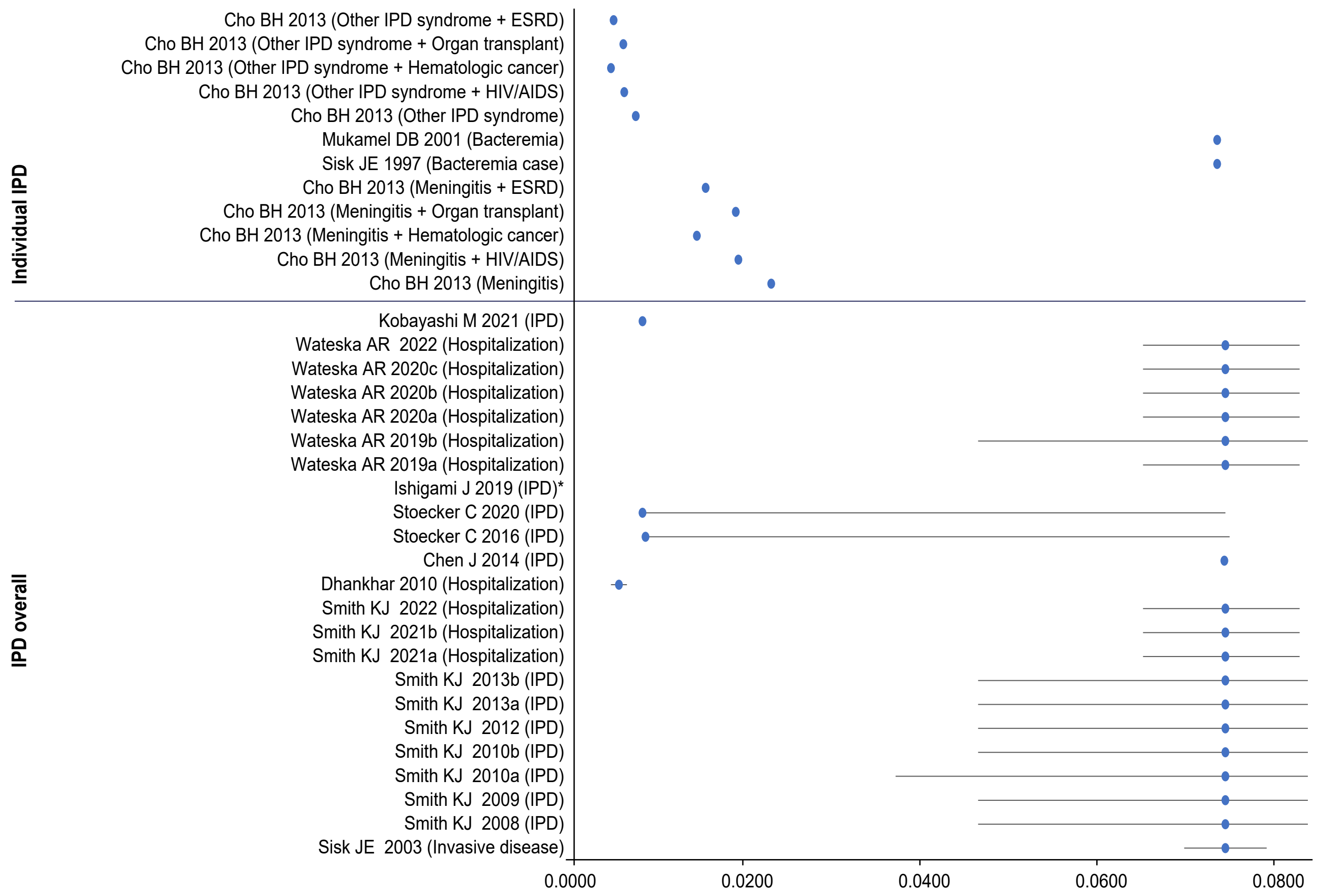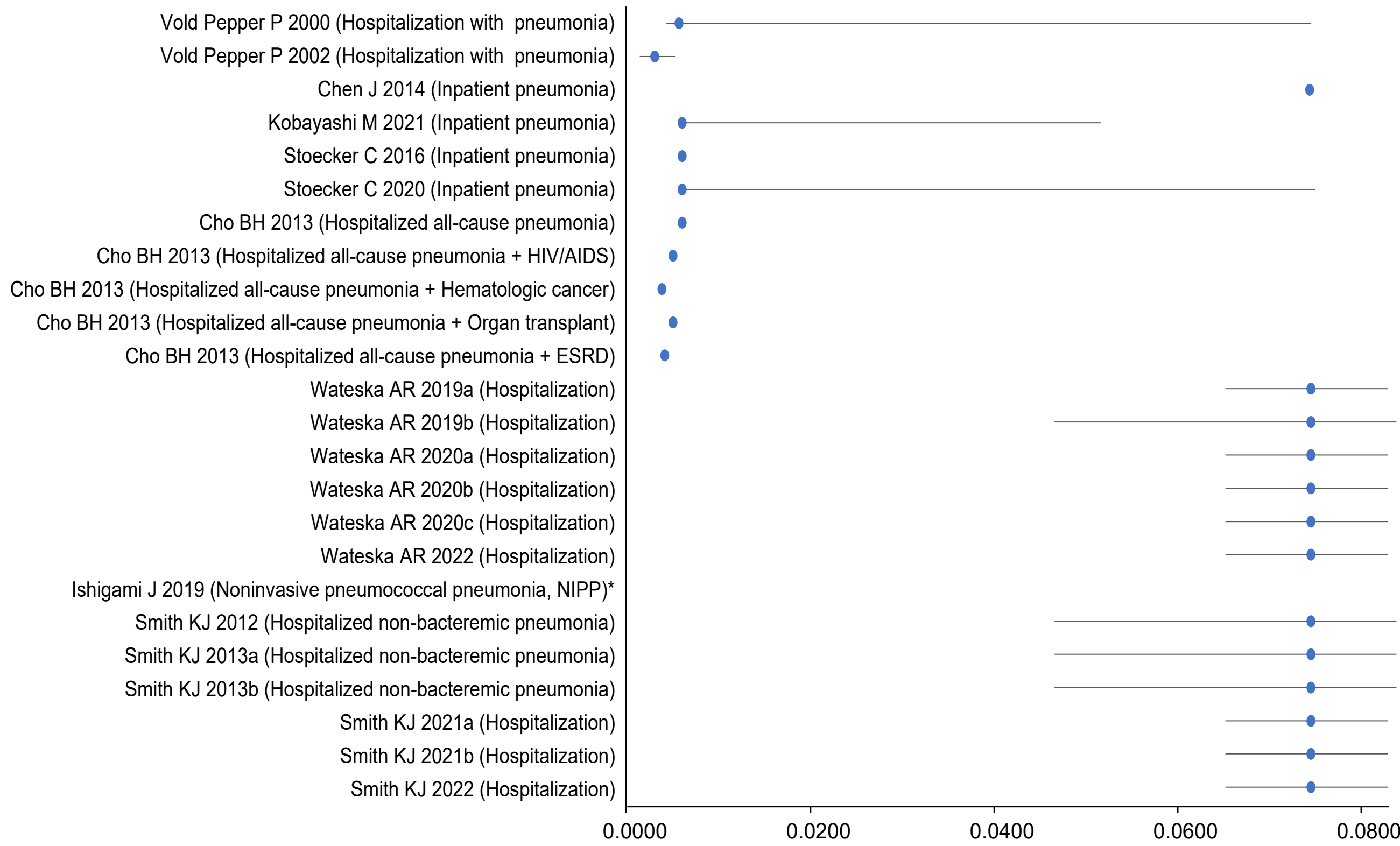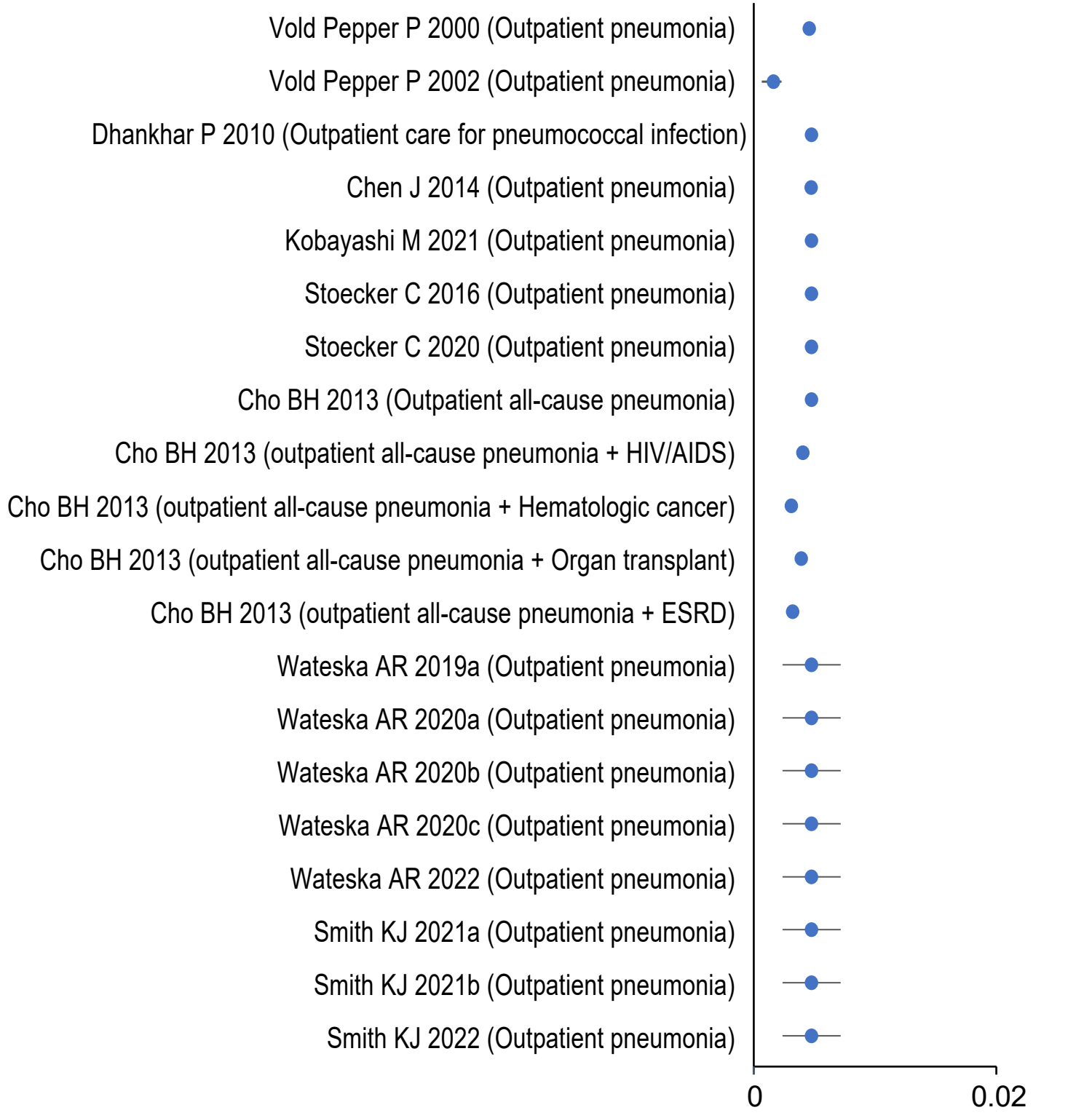### Figure 2. QALY decrements associated with inpatient pneumonia

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QALY, quality-adjusted life-year; IPD, invasive pneumococcal disease; HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; ESRD, end-stage renal disease; NIPP, noninvasive pneumococcal pneumonia; CEA, cost-effectiveness analysis.
The base-case value and the range in the sensitivity analysis (if reported) were presented for the derived/reported QALY decrement from each CEA.
* Ishigami J applied a QALY decrement of 0.8 for the base case and a range of 0.5-0.9 in the CEA, which was an outlier not displayed in the figure.

Figure 3. QALY decrements associated with outpatient pneumonia

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QALY, quality-adjusted life-year; HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; ESRD, end-stage renal disease.
The base-case value and the range in the sensitivity analysis (if reported) were presented for the derived/reported QALY decrement from each CEA.

Conclusions

- Utility inputs varied substantially in the published CEAs of pneumococcal vaccines in adults in the US, and most of the CEAs referenced other CEAs for these inputs
- Model inputs for health state utilities or QALY decrements associated with IPD, inpatient and outpatient pneumonia, and PMS were sourced from a limited number of original studies
- None of the original studies estimated utilities of PD in adults
- The utilities were applied to the CEAs with strong assumptions
- A significant research gap exists regarding health utilities of PD in the US adult population, which warrants future studies to provide more accurate health-related utilities of PD in this population

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