Cost-Effectiveness of 20-Valent Pneumococcal Conjugate Vaccine Among US Children with Underlying Medical Conditions

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ABSTRACT

***Introduction*:** A 20-valent pneumococcal conjugate vaccine (PCV20) was recently recommended for use among US children. We evaluated the cost-effectiveness of PCV20 among children aged 6 years with chronic medical conditions (CMC+) and children aged 6 years with immunocompromising conditions (IC) versus one and two doses of 23-valent pneumococcal polysaccharide vaccine (PPSV23), respectively.

***Methods*:** A probabilistic model was employed to depict 10-year risk of clinical outcomes and economic costs of pneumococcal disease, reduction in life years from premature death, and expected impact of vaccination among one cohort of children with CMC+ and IC aged 6 years. Vaccine uptake was assumed to be 20% for both PCV20 and PPSV23. Cost per quality-adjusted life year (QALY) gained was evaluated from the US societal and healthcare system perspectives; deterministic and probabilistic sensitivity analyses (DSA/PSA) were also conducted.

***Results*:** Among the 226,817 children with CMC+ aged 6 years in the US, use of PCV20 (in lieu of PPSV23) was projected to reduce the number cases of pneumococcal disease by 5203 cases, medical costs by US$8.7 million, and nonmedical costs by US$6.2 million. PCV20 was the dominant strategy versus PPSV23 from both the healthcare and societal perspectives. In the PSA, 99.9% of the 1000 simulations yielded a finding of dominance for PCV20. Findings in analyses of children with IC aged 6 years in the USA were comparable (i.e., PCV20 was the dominant vaccination strategy). Scenario analyses showed that increasing PCV20 uptake to 100% could potentially prevent > 22,000 additional cases of pneumococcal disease and further reduce medical and nonmedical costs by US$70.0 million among children with CMC+ and IC.

***Conclusions*:** Use of PCV20 among young children with CMC+ and IC in the USA would reduce the clinical burden of pneumococcal disease and yield overall cost savings from both the

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US healthcare system and societal perspectives. Higher PCV20 uptake could further reduce the number of pneumococcal disease cases in this population.

Keywords: Children; Costs and cost analysis; Immunization; Pneumonia; *Streptococcus pneumoniae*; Vaccination; Vaccines; Conjugate

Key Summary Points

Why carry out this study?

Until recently, the US Center for Disease Control (CDC) recommended the 23-valent pneumococcal polysaccharide vaccine (PPSV23) for children aged 2–18 years with underlying medical conditions.

PCV20 was recently approved by the Food and Drug Administration (FDA) for use among children and has been recommended by the ACIP for use among US infants as well as for children with underlying medical conditions.

This study evaluated whether PCV20 use would be cost effective compared with PPSV23 among young children with underlying medical conditions.

What was learned from the study?

Findings suggest that use of PCV20 (versus PPSV23) would markedly reduce the burden of pneumococcal disease among young children at elevated risk of pneumococcal disease and, thus, make an important contribution to pediatric public health.

Use of PCV20 among children with underlying medical conditions would reduce the clinical burden of pneumococcal disease and yield overall cost savings from both the US healthcare system and societal perspectives.

INTRODUCTION

Streptococcus pneumoniae causes significant morbidity and mortality in children of all ages, especially infants and those with underlying medical conditions [1]. Immunization is the principal means of preventing pneumococcal disease and is currently recommended for infants as well as toddlers, and older children aged ≤ 18 years with chronic medical conditions in the USA. The Advisory Committee on Immunization Practices (ACIP) has recommended pneumococcal vaccination for subgroups of US children since 1997 [2].

Infant vaccination with pneumococcal conjugate vaccines (PCVs) has proven extremely effective in reducing the risk of pneumococcal disease among young children [3]. Rates of IPD among children aged < 5 years in the US decreased by 93% between 1998 and 2019, which is largely credited to infant vaccination with 7-valent PCV (PCV7, introduced in 2000) and 13-valent PCV (PCV13, introduced in 2010) [3]. Despite considerable reductions in overall pediatric pneumococcus rates, children with underlying medical conditions remain at an elevated risk of pneumococcal disease [4]. Unpublished US CDC data presented at the February 2023 meeting of the ACIP show that risk of IPD among children aged < 5 years is 231× higher for those with hematologic malignancy (versus no condition) and 29× higher for those with sickle cell disease (versus no condition) [4].

Until recently, the US CDC recommended a single dose of 23-valent pneumococcal polysaccharide vaccine (PPSV23) for children aged 2–18 years with underlying medical conditions who have completed the infant PCV 3 + 1 series, as well as a second dose of PPSV23 5 years after the first dose for children with immunocompromising conditions [5]. To provide additional protection against pneumococcal disease, a novel 20-valent PCV (PCV20) was recently developed and approved for use in US adults aged 18 years and over, and more recently, children under the age of 18 years [6]. The additional seven vaccine serotypes in PCV20 (versus PCV13) were

targeted based on several factors, including associations with heightened disease severity, invasive potential, antibiotic resistance, and prevalence as a cause of pediatric and adult disease across widespread geographic areas in the post-PCV13 era [7–13].

As of June 2023, PCV20 is recommended for US infants under a 3 + 1 schedule, as well as for children with increased risk of pneumococcal disease [14]. This study evaluates the cost effectiveness of PCV20 versus previous vaccine recommendations (i.e., use of PPSV23) among US children aged 6 years with underlying medical conditions.

METHODS

Model Description

The model employs a probabilistic Markov framework to depict the risk of clinical outcomes and economic costs of pneumococcal disease over a 10-year time horizon (Fig. 1). The population at model entry comprises a single cohort of US children aged 6 years with underlying medical conditions at model entry and is stratified into those who are immunocompetent with chronic medical conditions (CMC+) and those who have immunocompromising conditions (IC); children are followed through age 15 years. Because the pediatric population aged 2–18 years with underlying conditions is heterogeneous with respect to age and condition, we selected 6-year-old children with one or more of
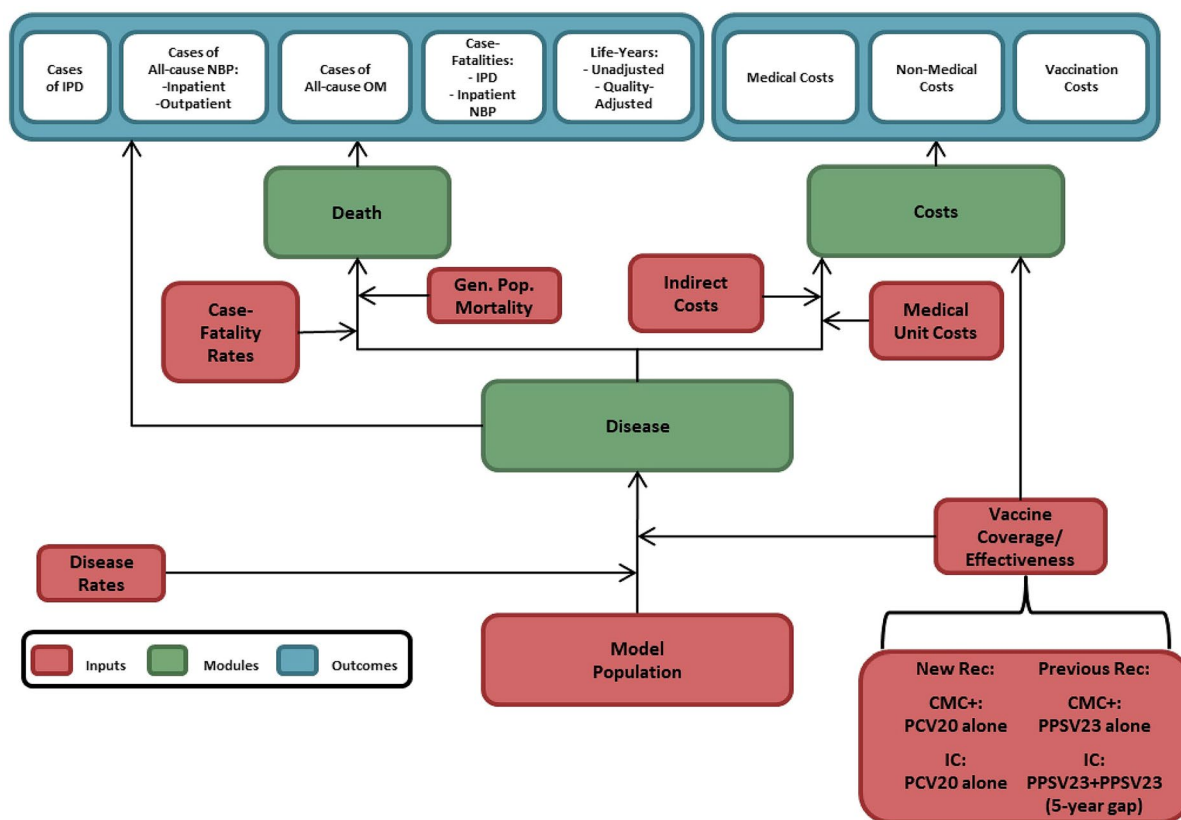
Fig. 1 A probabilistic Markov framework to depict the risk of clinical outcomes and economic costs of pneumococcal disease over a 10-year time horizon

the chronic medical or immunocompromising conditions included in the pneumococcal vaccine recommendations as the exemplar age for the population.

At model entry, 6-year-old children in the model population receive either PCV20 (intervention) or PPSV23 (standard of care). All children also are assumed to have received the 3 + 1 dose regimen of PCV13, as infants and are therefore (partially) protected (see below). For children with IC vaccinated with PPSV23 at model entry, a second dose of PPSV23 was provided 5 years after the first dose.

Expected clinical outcomes and economic costs are projected for the model population on an annual basis, based on age, risk profile (i.e., CMC+ versus IC), disease/fatality rates, PCV13 vaccination history, vaccination status/type (PCV20, PPSV23), and time since vaccination. Clinical outcomes include cases of invasive pneumococcal disease (IPD), all-cause nonbacteremic pneumonia (NBP), and all-cause otitis media (OM), as well as disease-associated death. IPD includes bacteremia and meningitis, all-cause NBP is stratified by setting of care (inpatient versus outpatient), and all-cause OM includes cases treated in all care settings. Children vaccinated at model entry, and those children who received PCV13 prior to model entry (assumed to be 100%), may be at lower risk of IPD, all-cause NBP, and all-cause OM. The magnitude of vaccine-associated risk reduction depends on clinical presentation, as well as the vaccine (effectiveness and serotype coverage), time since vaccination, and risk profile. The model assumes age-specific mortality due to IPD and all-cause NBP requiring inpatient care and other causes (i.e., other than IPD and all-cause NBP). All-cause NBP requiring outpatient care only and all-cause OM are assumed not to elevate risk of death.

Expected costs of medical treatment for IPD, all-cause NBP, and all-cause OM are generated based on event rates and unit costs in relation to the setting of care (i.e., inpatient versus outpatient) and age. Costs of vaccination—including the vaccine and its administration—are tallied at the time of administration. The value of morbidity- and mortality-related work loss is also tallied in the model.

Future life-years, QALYs, and costs are discounted in the base-case analysis, and both societal and healthcare system perspectives are employed.

Model Estimation

Model parameter values are summarized in Table 1. A detailed description of methods employed to estimate parameter values, along with tables reporting values employed in base-case analyses, scenario analyses, and probabilistic sensitivity analyses (PSA), are set forth in the supplemental material.

Model population: The model population included children with CMC+ (N = 226,817) and children with IC (N = 15,189) aged 6 years at model entry, estimated based on data from the US Census Bureau (number of US children aged 6 years) and a study by Pelton et al. (distribution of children by risk profile) [15, 16].

Disease rates: Age- and risk-specific rates of IPD, all-cause NBP, and all-cause OM were derived using age-specific rates and risk-specific relative rates/population weights from published studies [17–22]. From sources providing age-specific values, rates by single year of age from 6 to 15 years were calculated using techniques of linear interpolation between reported point estimates. Age-specific rates were then apportioned across risk groups based on relative rates and corresponding population weights [23].

Case-fatality and mortality rates: For IPD, age-specific values were calculated based on 2017–2019 Active Bacterial Core surveillance (ABCs) data [17]; for all-cause inpatient NBP, age-specific values were based on the CDC 15-valent PCV (PCV15) cost-effectiveness assessment and a published study [24–27]. The background mortality rate was calculated based on age-specific mortality rates among the general population and was downwardly adjusted to account for death due to IPD and inpatient NBP [28]. Case-fatality and mortality rates were assumed to be the same for children with CMC+ and IC.

Vaccine effectiveness: Vaccine effectiveness (VE) for PCV13 and PCV20 against vaccine-type IPD among children with CMC+ was based on the Moore et al. case–control study

Table 1 Model parameter values

	Age (years)									
	6	7	8	9	10	11	12	13	14	15
No. of children										
CMC+	2,26,817	–	–	–	–	–	–	–	–	–
IC	15,189	–	–	–	–	–	–	–	–	–
Annual disease rates (per 100,000)										
CMC+										
IPD	16.3	13.6	10.8	8.7	6.9	5.3	4.8	4.9	5.1	5.3
All-cause NBP										
Inpatient	1149	1036	921	814	712	612	782	792	801	812
Outpatient	7385	6574	5750	4980	4241	3517	3382	3298	3216	3139
All-cause OM	48,534	42,646	36,736	30,978	25,304	19,674	20,389	19,791	19,198	18,616
IC										
IPD	198.5	165.9	132.0	106.0	84.5	65.3	58.6	60.2	62.0	64.3
All-cause NBP										
Inpatient	2786	2512	2233	1974	1726	1483	1897	1920	1943	1969
Outpatient	17,910	15,941	13,944	12,077	10,285	8530	8202	7998	7800	7612
All-cause OM	48,534	42,646	36,736	30,978	25,304	19,674	20,389	19,791	19,198	18,616
Case fatality rates (per 100)										
IPD	3.9	4.0	4.2	4.3	4.5	4.6	4.6	4.6	4.7	4.7
All-cause inpatient NPB	0.8	0.9	1.0	1.1	1.2	1.3	1.3	1.3	1.3	1.3
Medical costs (US dollars)										
IPD	$55,963	$55,963	$55,963	$55,963	$55,963	$55,963	$55,963	$55,963	$55,963	$55,963
All-cause NBP										
Inpatient	$20,596	$20,596	$20,596	$20,596	$20,596	$20,596	$20,596	$20,596	$20,596	$20,596

Table 1 continued

	Age (years)									
	6	7	8	9	10	11	12	13	14	15
Outpatient	$693	$693	$693	$693	$693	$693	$693	$693	$693	$693
OM	$232	$232	$232	$232	$232	$232	$232	$232	$232	$232
Nonmedical costs (US dollars)[a]										
IPD	$3042	$3042	$3042	$3042	$3042	$3042	$3042	$3042	$3042	$3042
All-cause NBP										
Inpatient	$2012	$2012	$2012	$2012	$2012	$2012	$2012	$2012	$2012	$2012
Outpatient	$431	$431	$431	$431	$431	$431	$431	$431	$431	$431
OM	$949	$949	$949	$949	$949	$949	$949	$949	$949	$949
Vaccine price (US dollars)[b]										
PCV20	$204.32	–	–	–	–	–	–	–	–	–
PPSV23	$83.75	–	–	–	–	–	–	–	–	–
Utilities and disutilities										
General population utility	0.93	0.93	0.93	0.93	0.93	0.93	0.93	0.93	0.93	0.93
Disutilities										
IPD	0.009	0.009	0.009	0.009	0.009	0.009	0.009	0.009	0.009	0.009
All-cause NBP										
Inpatient	0.006	0.006	0.006	0.006	0.006	0.006	0.006	0.006	0.006	0.006
Outpatient	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004
OM	0.005	0.005	0.005	0.005	0.005	0.005	0.005	0.005	0.005	0.005

CMC+ immunocompetent with chronic medical conditions, *IC* immunocompromised, *IPD* invasive pneumococcal disease, *NBP* nonbacteremic pneumonia, *OM* otitis media, *PCV20* 20-valent pneumococcal conjugate vaccine, *PPSV23* pneumococcal polysaccharide vaccine

[a]Value of caregiver productivity loss

[b]Vaccine prices were based on 2023 private and Vaccines for Children (VFC). Program values, along with corresponding weights (35% and 65%). Vaccine administration cost was assumed to be $17.63

of PCV13 (≥ one dose) among US children aged 2–59 months, which demonstrated effectiveness of 86.0% [95% confidence interval (CI) 75.5–92.3%] (Fig. 2) [29]. VE-PPSV23 against VT-IPD among children with CMC+ was assumed to be 63.0% based on Fiore et al. [30]. VE-PCV20 and VE-PCV13 versus all-cause noninvasive disease among children with CMC+ was estimated by multiplying the effectiveness estimates of inpatient NBP (25.5%), all-cause ambulatory NBP (6.0%), and all-cause OM (7.8%) from the PCV7 pivotal trial with the ratio of current serotype coverage level for each vaccine to serotype coverage level for PCV7 (80.6%) in the 2000 calendar year (i.e., the year PCV7 was introduced in the USA) [31–33]. VE-PPSV23 against NBP and OM was assumed to be 0% based on various published sources and consistent with base-case assumptions employed in a number of economic studies [34–49]. For children with IC, VE-PCV20 and VE-PPSV23 were reduced by 15.6% relative to corresponding values for children with CMC+, based on the ratio of VE-PCV7 against VT-IPD for children with comorbidities (81%) versus healthy children (96%) from Whitney et al. [50].

Age-specific proportions of invasive disease attributable to vaccine serotypes were sourced from 2019 ABCs data, reduced due to herd effects from projected use of PCV20 among infants, and assumed to be the same for children with CMC+ and IC. Age-specific proportions for noninvasive disease were assumed to be the same as those for invasive disease; additional details are provided in Supplemental Material [51]. It was assumed that VE-PCV would persist
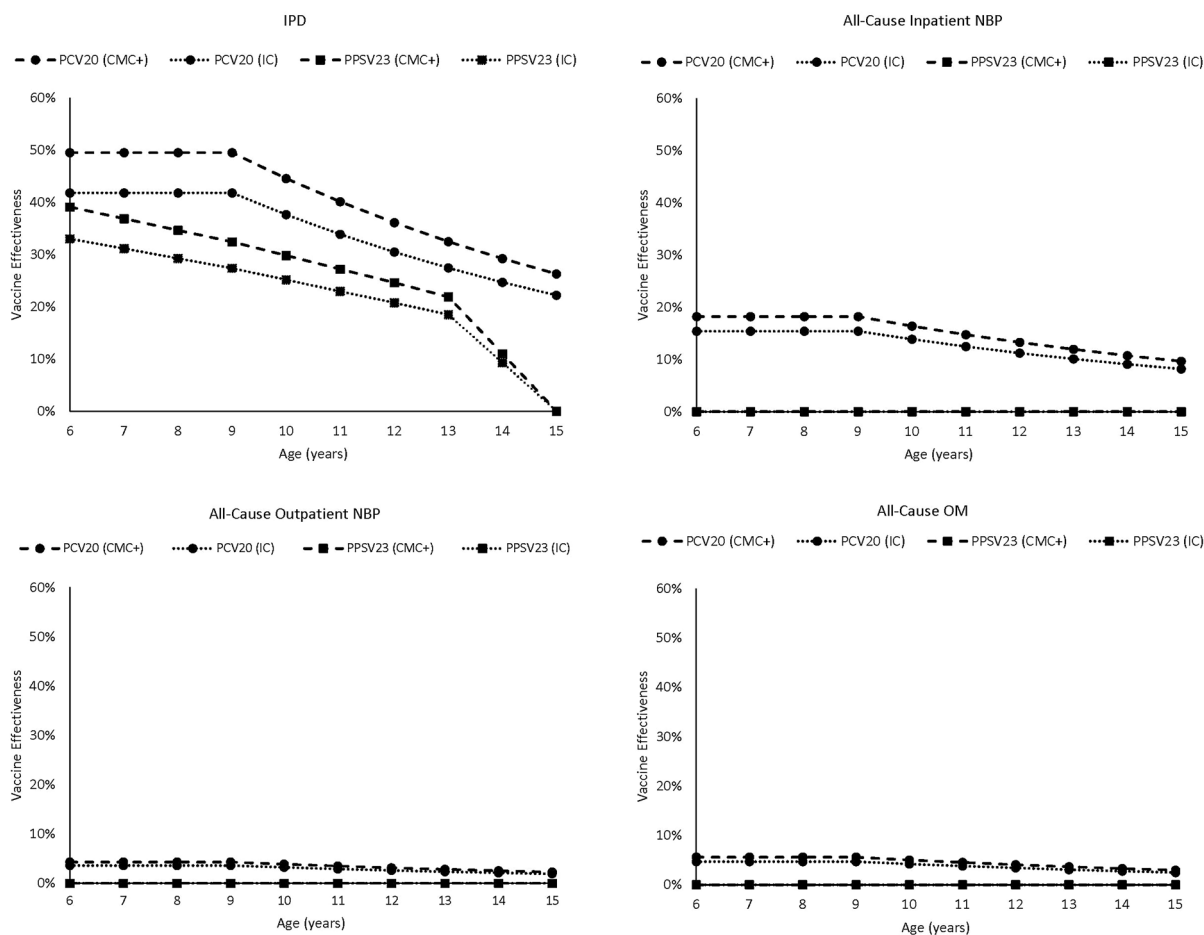

Fig. 2 Effectiveness of PCV20 and PPSV23 among children with CMC+ and IC

at the initial level for 4 years and, thereafter, was subject to 10% exponential decay annually. For PPSV23, VE was assumed to wane based on data reported by Djennad et al. [52]. Serotype replacement was assumed not to occur.

Medical and nonmedical costs: Costs of medical treatment for IPD, all-cause inpatient NBP, and all-cause outpatient NBP were based on retrospective healthcare claims studies by Weycker et al. [53]. Cost of OM (all care settings) was based on reported values in a study by Tong et al. [22]. Unit costs were assumed to be the same in the CMC+ and IC populations. Costs of medical treatment were inflated to 2022 US dollars (USD) using the Consumer Price Index for medical care [54]. Prices of vaccines (per dose) are set forth in Table 1. Nonmedical costs per episode of disease were estimated based on productivity loss incurred by caregivers of infected children [17, 55–57]. A human capital approach was employed to estimate indirect costs, which were based on work force participation, work loss days, and average daily salary [58–60].

Utilities and disutilities: General population utility for children aged 6–15 years was assumed to be 0.93, based on EQ-5D-5L population norms for persons aged 5–19 years [61]. Baseline utility values were assumed to be the same across risk groups. Disease-related utility decrements were taken from published cost-effectiveness analyses of PCVs and were assumed to be invariant by age [62–64]. Because disutility varies for meningitis (0.0232) and bacteremia (0.0079), a single estimate for all IPD was derived based on the weighted average of disutilities (i.e., assuming 7% meningitis and 93% bacteremia) [17].

Analyses

Cost-effectiveness of PCV20 [versus PPSV23 (CMC+, one dose and IC, two dose)] was calculated in terms of the cost per QALY gained, based on the ratio of the difference in total costs to the difference in total QALYs. Costs and QALYs were discounted at a rate of 3% per annum [65]. Vaccine uptake at model entry was assumed to be 20% among each population subgroup, irrespective of vaccination strategy [66]. In addition, all children in the model were assumed to have received PCV13 prior to model entry [67]. One-way deterministic sensitivity analyses (±25% of the base-case values), scenario analyses, and PSAs (1000 replications) were also conducted; additional details on scenario analyses and the PSAs are set forth in the supplemental material. A US healthcare system perspective [including direct (i.e., medical and vaccination) costs] and societal perspective [including direct and indirect (i.e., productivity loss-related) costs] were employed.

Ethics Approval

Human subjects did not participate in this study; thus, ethical approval was not required and informed consent was not applicable.

RESULTS

Immunocompetent Children with Chronic Medical Conditions

Base-case analysis: Use of PCV20 (in lieu of PPSV23) among children with CMC+ aged 6 years (*N* = 226,817) was projected—during the 10-year modeling horizon—to reduce IPD cases by 4, all-cause inpatient NBP by 392, all-cause outpatient NBP by 516, all-cause OM cases by 4291, disease-related deaths by 4, medical costs by US$8.7 million, and nonmedical costs by US$6.2 million (Table 2). Although vaccination costs were higher with PCV20 (by US$5.5 million), they were offset by reductions in medical and nonmedical costs, yielding cost savings of US$3.2 million from the healthcare system perspective and US$9.4 million from the societal perspective. Use of PCV20 was therefore projected to dominate PPSV23 (i.e., to yield higher QALYs and lower costs) from the US societal and healthcare system perspectives.

Deterministic sensitivity, scenario, and probabilistic sensitivity analyses

In all one-way deterministic sensitivity analyses PCV20 remained dominant versus PPSV23 (Supplementary Table 19). Additionally, in

Table 2 Projected clinical outcomes and economic costs with use of PCV20 versus PPSV23 among children with CMC+ and IC aged 6 years

	Children with CMC+			Children with IC		
	PPSV23	PCV20	Difference	PPSV23[a]	PCV20	Difference
Clinical outcomes (no.)						
Cases of disease						
IPD	151.9	148.3	− 3.6	127.5	125.8	− 1.7
All-cause NBP						
Inpatient	18,224.1	17,832.3	− 391.8	2979.7	2926.1	− 53.6
Outpatient	1,01,913.4	1,01,397.5	− 515.9	16,570.2	16,499.7	− 70.5
All-cause OM	6,29,463.0	6,25,171.6	− 4291.4	42,225.7	41,983.7	− 242.0
Disease-related deaths	209.0	204.7	− 4.4	38.6	37.9	− 0.6
Economic costs ($) (millions)						
Vaccination + administration	4.6	10.1	5.5	0.6	0.7	0.1
Medical	536.0	527.3	− 8.7	80.1	78.9	− 1.2
Non-medical	534.4	528.2	− 6.2	58.5	57.8	− 0.7
Total (medical + non-medical)	1070.4	1055.5	− 14.9	138.6	136.7	− 1.9
Life years (no.)						
Unadjusted (LYs)	54,99,417.2	54,99,504.6	87.4	3,67,782.9	3,67,796.0	13.1
Quality-adjusted (QALYs)	49,28,161.6	49,28,263.1	101.5	3,29,536.5	3,29,549.8	13.3
Cost per QALY	–	–	Dominant	–	–	Dominant
Cost per LY	–	–	Dominant	–	–	Dominant

CMC+ immunocompetent with chronic medical conditions, *IC* immunocompromised, *IPD* invasive pneumococcal disease, *LYs* life years, *NBP* nonbacteremic pneumonia, *OM* otitis media, *PCV20* 20-valent pneumococcal conjugate vaccine, *PPSV23* pneumococcal polysaccharide vaccine, *QALYs* quality-adjusted life years

[a]For children with IC, PPSV23 was administered at model entry and again 5 years later

scenario analyses employing alternative values for disease-related disutilities, reduced direct effectiveness of PCV against serotype 3, no history of PCV13 use, and higher (100%) PCV20 uptake, PCV20 dominated PPSV23 (Supplementary Tables 20–23). In the PSA, 99.9% of the 1000 simulations yielded estimates of cost per QALY gained that were in the southeast quadrant of the scatterplot, indicating lower costs and higher QALYs—and thus dominance—with PCV20 (Fig. 3).

Immunocompromised Children

Base-case analysis: Use of PCV20 (in lieu of two doses of PPSV23) among children with IC aged 6 years (*N* = 15,189) was projected—during the 10-year modeling horizon—to reduce IPD cases by 2, all-cause inpatient NBP by 54, all-cause outpatient NBP by 70, all-cause OM cases by 242, disease-related deaths by 1, medical costs
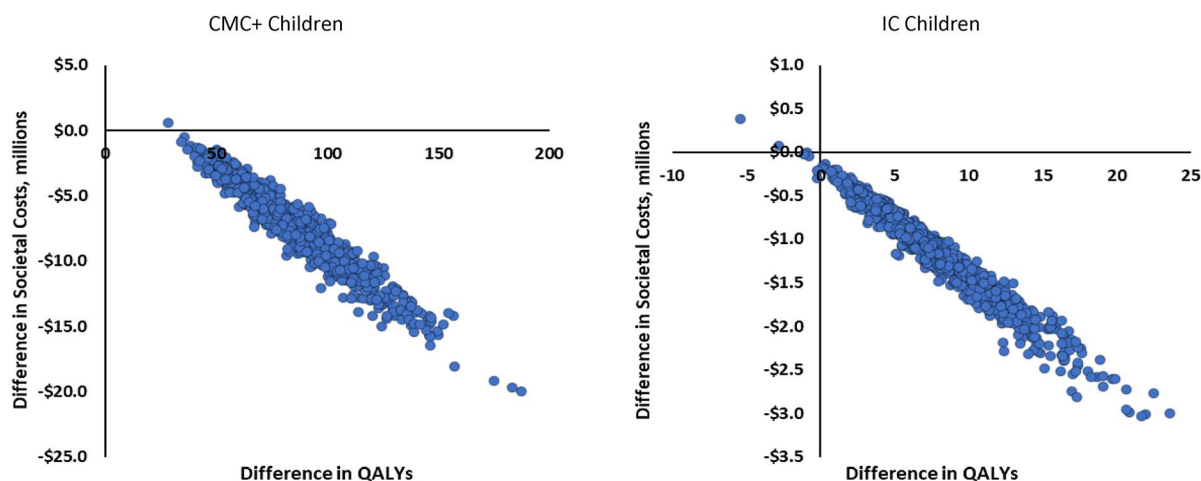
Fig. 3 Results from probabilistic sensitivity analyses of PCV20 versus PPSV23 from the US societal perspective

by US\$1.2 million, and nonmedical costs by \$0.7 million (Table 2). Although vaccination costs were higher with PCV20 (by US\$0.1 million), they were offset by reductions in medical and nonmedical costs, yielding cost savings of US\$1.1 million from the healthcare system perspective and US\$1.8 million from the societal perspective. Use of PCV20 was, therefore, projected to dominate PPSV23 from the US societal and healthcare system perspectives.

Deterministic sensitivity, scenario, and probabilistic sensitivity analyses: In all one-way deterministic sensitivity analyses, PCV20 remained dominant versus PPSV23 (Supplementary Table 19). Additionally, in scenario analyses employing alternative values for disease-related disutilities, reduced direct effectiveness of PCV against serotype 3, no history of PCV13 use, and higher (100%) PCV20 uptake, PCV20 dominated PPSV23 (Supplementary Tables 20–23). In the PSA, 97.3% of the 1000 simulations yielded estimates of cost per QALY gained that were in the southeast quadrant of the scatterplot, indicating lower costs and higher QALYs—and thus dominance—with PCV20 (Fig. 3).

DISCUSSION

This is the first cost-effectiveness study evaluating the impact of PCV20 use among US children with underlying comorbidities. In this study, we employed a probabilistic model with a Markov-type process to evaluate the public health and economic impact of PCV20 (versus PPSV23) among US children aged 6 years with underlying medical conditions. Study findings indicated that—under reasonable assumptions, and variations thereof, concerning disease burden, vaccine effectiveness, and vaccine cost—use of PCV20 among young children with CMC+ and IC would reduce the clinical burden and overall economic costs [direct (including vaccination) and indirect] of pneumococcal disease and, thus, would be a dominant vaccination strategy versus previous vaccination recommendations. Compared with PPSV23, PCV20 would prevent almost 400 hospitalizations for pneumococcal disease and about 4800 ambulatory encounters for pneumococcal disease among children with CMC+ aged 6 years in the US. Moreover, incremental acquisition costs of PCV20 were fully offset by savings from averted disease, yielding US\$9.4 million in net

savings from the societal perspective. The same trend was observed when comparing PCV20 versus PPSV23 among children with IC aged 6 years. It is important to interpret the findings of our analysis with caution, as the cohort under analysis omits 2–5- and 7–18-year-olds; vaccine use across the pediatric risk groups would result in much broader public health impact. Study findings therefore support the adoption of recent CDC recommendations for use of PCV20 among children with CMC+ and IC aged 2–18 years who have a history of use of PCV15 or PCV13 [14].

While the economic benefits of PCV20 were somewhat lower from a healthcare system perspective, PCV20 remained dominant versus PPSV23 for both children CMC+ and IC. Deterministic sensitivity, scenario, and probabilistic sensitivity analyses yielded the same findings as base-case analyses (i.e., lower costs and higher QALYs with PCV20). Importantly, if recommendation of the simpler, single dose PCV20 strategy led to higher vaccine uptake among children with CMC+ and IC, disease burden and medical and nonmedical costs could be further reduced (cases by 22,314 and costs by US$70.0 million).

While this study is, to the best of our knowledge, the first peer-reviewed economic evaluation of PCV20 in young children with underlying medical conditions, the findings described herein are consistent with other recent studies presented during the June 22, 2023 ACIP meeting [68, 69]. Both models presented during the meeting (i.e., Stoecker et al. and Huang et al.) showed that vaccination of children with CMC+ or children with IC with PCV20 was cost saving compared with vaccination with the PCV13 + PPSV23 series. PCV20 was also found to be cost saving in both models when compared with the PCV15 + PPSV23 series.

Some limitations of the study should be noted. While the CDC recommendations considered herein are applicable to children with CMC+ or IC aged ≥ 2 years who previously received PCV13, our model population was limited to children aged 6 years (which was assumed to be a "representative" age for the CMC+ and IC population aged 2–18 years). Nevertheless, when we ran the analyses for 12-year-olds, the conclusion remained unchanged (results not shown).

Although age-specific disease rates and costs were employed in the model, we note that the US pediatric population and healthcare delivery system are highly heterogeneous, and thus, the generalizability of results may be limited. We also note that recent infant recommendations include optional use of PCV15 in the 3 + 1 schedule (i.e., in lieu of PCV13), which means that in the future, some children aged 2–18 years may be protected against serotypes 22F and 33F through the infant vaccination series. Nonetheless, it is our expectation that the incremental benefit of PCV20 administered during early childhood would remain substantial.

Perhaps the greatest area of uncertainty concerns our estimates of vaccine effectiveness. Consistent with findings from PPSV23 effectiveness studies published over the past 30 years, as well as a number of previously published cost-effectiveness analyses of pneumococcal vaccination, we assumed PPSV23 provides protection against IPD only [34–49, 70–73]. Although recently published data suggest that PPSV23 may provide some level of protection against NBP, the quality of evidence generated via these retrospective evaluations is not yet sufficient to warrant a different assumption [74, 75].

Estimates of the effectiveness of PCVs for children aged 6–15 years are not currently available in published literature. However, based on the study by Whitney et al. [50] in which there was little variation in VE by age [i.e., VE with one dose of PCV7 at age ≥ 24 months was 94% (95% CI 49–99%) and VE among children aged 12–23 months receiving 1 dose of PCV7 was 93% (95% CI 68–98%)], we assumed initial effectiveness of PCVs among children aged 6 years to be the same as that for children aged 2–59 months reported by Moore et al. [29]. Moreover, because clinical trials have not been conducted for PCV20, VE-PCV20 was derived using data from a variety of sources, with the process of interpretation and synthesis potentially subject to bias. However, the approach employed to estimate vaccine effectiveness for PCV20 was robust, using the best available evidence, and was consistent with previous research. Furthermore, it was assumed that vaccine serotype coverage for IPD was generalizable to noninvasive

diseases, an appropriate assumption given the lack of data to suggest otherwise.

In the absence of evidence on the duration of protection for PCV20, we assumed that the duration of protection would be the same as that for PCV13, which is aligned with the assumption that initial VE-PCV20 versus vaccine-type disease is the same as that for PCV13. We assumed a stable duration of protection for 4 years based on a study by Savulescu et al. [76]. After 4 years, we conservatively assumed an annual waning rate of 10% relative to the prior year (i.e., exponential decay). For this reason, the full benefits of PCV20 vaccination (i.e., those beyond 10 years) may be underestimated.

Our model, like all such health economic models, simplifies reality to some extent. Our model does not, for example, consider possible indirect effects of vaccination within (or outside) the population of interest or broader societal benefits that may be conferred by vaccines (e.g., reducing antimicrobial resistance or reducing use of antibiotics). Finally, our model did not include other potential downstream adverse outcomes and costs associated with pneumonia, which confers a conservative bias against use of PCV20.

CONCLUSIONS

The results of this evaluation suggest that use of PCV20—in lieu of PPSV23—would yield important reductions in the clinical burden of pneumococcal disease among children with CMC+ and IC conditions as well as net savings from both the US societal and healthcare system perspectives. Accordingly, use of PCV20 in this population would have a favorable impact on individual patients and public health, as well as is a good use of resources in the US. Moreover, higher PCV20 uptake in this population could substantially increase the number of pneumococcal disease cases averted through vaccination.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Ethical Approval. Human subjects did not participate in this study; thus, ethical approval was not required and informed consent was not applicable.

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