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Cost-Effectiveness Analysis of PCV20 3+1 Versus PCV15 2+1 Vaccination of the Pediatric Population in the Netherlands

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INTRODUCTION

- The Dutch pediatric National Immunization Program (NIP) has included the pneumococcal conjugate vaccine (PCV) with valency of 10 (PCV10) since 2011.[1] However, increases in pneumococcal disease due to non-PCV10 serotypes indicate a need for higher-valent vaccines.[2]
- In December 2024, the Netherlands will incorporate the 15-valent PCV (PCV15) under a 2+1 schedule into the pediatric NIP, while the 20-valent PCV (PCV20), approved by the European Medicines Agency in March 2024 under a 3+1 schedule, is not yet included.[3,4]

OBJECTIVE

- This study examined the cost-effectiveness of implementing PCV20 under a 3+1 schedule versus PCV15 under a 2+1 schedule in the Dutch pediatric NIP.

METHODS

- The analysis employed a Markov multiple-cohort model with annual cycles over a 10-year time horizon from a societal perspective with annual discount rates of 1.5% (benefits) and 3.0% (costs) as per Zorginstituut Nederland guidelines.[5]
- The model encompassed clinical events: invasive pneumococcal disease (IPD), hospitalized and non-hospitalized pneumonia, otitis media (OM), a non-disease state, and death.
- The vaccinated cohort included infants aged <2 years, with 12-month stratification for children aged <5 years and broader groups for older individuals to allow for age-specific variations in event probabilities, utilities, costs, and mortality rates.
- Parameters including epidemiology, serotype coverage, cost, and quality of life were informed by Dutch-specific sources (**Table 1**).[2,6-17]
- Direct effects benefited the vaccinated cohort, and indirect effects benefited the entire population (**Table 2**). Direct effects against IPD were Dutch-specific data from RIVM,[2] and direct effects against non-invasive disease from 7-valent PCV (PCV7) trials.[18-22] Indirect effects were based on PCV10/13-valent PCV (PCV13) effectiveness, PCV7 efficacy, and PCV13 impact data.[18-24]
- Model outcomes included disease cases, deaths, medical cost of doses, medical cost of disease, societal costs (travel cost and productivity loss), life-years (LY), quality-adjusted life years (QALY), and incremental cost-effectiveness ratios (ICER).
- Model robustness was evaluated through deterministic sensitivity analyses (DSA), probabilistic sensitivity analyses (PSA), and a series of additional scenario assessments.

Table 1. Key inputs

Input	Age, y	IPD		Hospitalized pneumonia	Non-hospitalized pneumonia	OM
		Meningitis	Bacteremia			
Incidence per 100,000 individuals[2,6]	<5	8.6		237	1,726	7,734
	5–17	3.7		67	497	
	18–49			50	468	-
	50–64	14.7		127	992	-
	≥65	35.7		449	2,895	-
Fatality rate,[2,7] %	<5	7.0	7.0	1.4	-	-
	5–17			1.1	-	-
	18–49			0.9	-	-
	50–64			3.0	-	-
	≥65			15.2	-	-
Medical costs per episode,[8,9] €	<2	12,161.93	6,668.90	3,350.68	624.67	24.69
	2–4	9,061.66	1,984.54			
	5–17	10,250.26	4,960.99	4,080.66	650.59	-
	18–49	11,652.53	13,001.02	7,398.01	937.01	-
	50–64	26,575.12	13,699.32	7,982.23	1,053.65	-
	≥65	25,533.03	10,275.55	7,625.36	1,061.64	-
Societal costs (productivity loss),[8-10] €	<1	3,837.25	2,257.21	808.08	225.72	225.72
	1–4	2,257.21	790.02			
	5–17	3,160.09	3,385.81	907.40		-
	18–49	6,320.18	6,771.62	2,090.17		-
	50–64	10,834.60	7,223.07	2,695.11		-
	≥65	10,383.16	6,997.34	3,322.61		-
Utility decrements[11-16]	<18	0.023	0.008	0.006	0.004	0.005
	≥18	0.13	0.13	0.13	0.045	-
	Vaccine	Age <5 y	Age 5–49 y	Age 50–64 y	Age ≥65 y	-
Current serotype distribution by vaccine,[2] %	PCV15	64.1	50.4	54.3	53.9	-
	PCV20	78.4	77.6	81.5	74.2	-
	Age, y	**PCV15**		**PCV20**		
Cost of dose,[18] €	All ages	68.56		76.10		
Administration cost per dose,[19] €	All ages	12.81		12.81		
Travel cost per dose,[20] €	All ages	4.81		4.81		

Abbreviations: IPD, invasive pneumococcal disease; OM, otitis media; PCV, pneumococcal conjugate vaccine; y, years.

Table 2. Vaccine effectiveness inputs

		Year					
		1	2	3	4	5	6–10
Indirect effect – ramp-up (PCV15/PCV20),[21,22] %		0.0	37.5	52.8	67.7	82.7	100.0
	Age group, years	**IPD[21,22]**		**Hospitalized pneumonia[†22,23,24,25]**	**Non-hospitalized pneumonia[†22,23,24,25]**	**OM[§22,26]**	
Indirect effects, %	<17	83.0		30.5	25.5	20.0	
	18–49	83.0		15.0	0.0	-	
	50–64	77.0		15.0	0.0	-	
	≥65	73.0		15.0	0.0	-	
		IPD[2]		**Hospitalized pneumonia[27]**	**Non-hospitalized pneumonia[28]**	**OM[28]**	
Direct effects,[‡] %		88.0		25.5	6.0	7.8	

Indirect vaccine impact data were adjusted using serotype coverage pre-PCV13 to current era for higher-valent vaccines. †For children, Levy et al. 2017[23] data were adjusted using Janoir et al. 2016[24] IPD serotype distribution at PCV13 introduction in 2009. For adults, Rodrigo et al. 2015[25] data were similarly adjusted using the distribution from Ladhani et al. 2018.[22] §Data from Lau et al. 2015[26] were adjusted for IPD serotype distribution by Ladhani et al. 2018[22] at PCV13 introduction in 2009. ‡Direct vaccine efficacy data were adjusted using serotype coverage pre-PCV7 to current year for higher-valent vaccines. PCV7 all-cause efficacy data were adjusted for pre-PCV7 era (80.6% PCV7 serotype coverage) to pre-PCV20 era for PCV20 (47.5%) and PCV15 (17.8%); Pfizer data on file. Abbreviations: IPD, invasive pneumococcal disease; OM, otitis media; PCV, pneumococcal conjugate vaccine.

RESULTS

Table 3. Base-case results

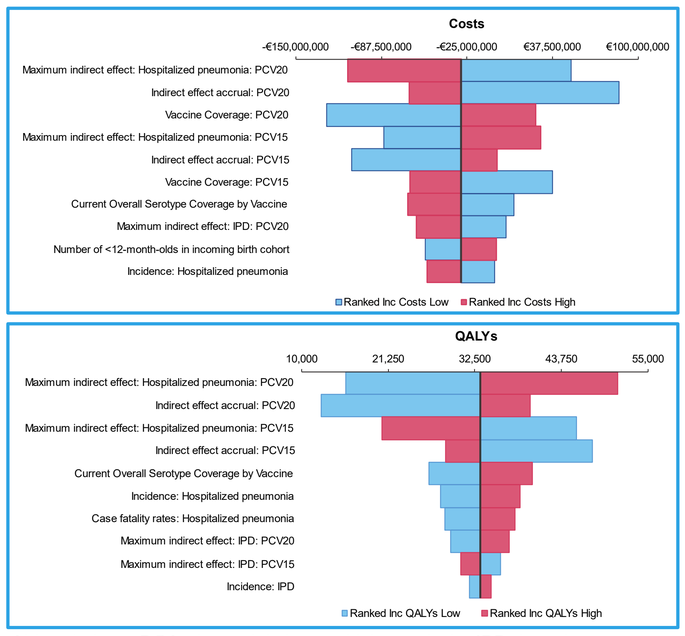
Model outcomes	PCV15 2+1	PCV20 3+1	Incremental
Cases of IPD	17,936	14,492	-3,444
Cases of hospitalized pneumonia	284,079	268,783	-15,296
Cases of non-hospitalized pneumonia	2,232,683	2,220,257	-12,426
Cases of OM	567,895	541,403	-26,492
Number of deaths due to disease	28,406	26,845	-1,561
Total QALYs	533,892,524	533,925,756	33,232
Total LYs	617,587,557	617,606,738	19,180
Total medical cost of doses	€340,639,758	€496,273,984	€155,634,226
Total medical cost of disease	€3,940,362,200	€3,810,249,190	-€130,113,010
Total travel costs of administration	€20,118,628	€26,824,884	€6,706,256
Total societal cost of disease (productivity loss)	€1,367,808,378	€1,306,215,210	-€61,593,168
Total costs	€5,668,928,964	€5,639,563,268	-€29,365,696
ICER per QALY	-	-	PCV20 is dominant

Abbreviations: ICER, incremental cost-effectiveness ratio; IPD, invasive pneumococcal disease; LY, life-year; OM, otitis media; PCV, pneumococcal conjugate vaccine; QALY, quality-adjusted life year.

Base-case results

- PCV20 was estimated to reduce more of the clinical and economic burden of pneumococcal disease than PCV15, resulting in cost-savings and QALY gains, making it the dominant strategy (**Table 3**).
- Despite the additional vaccination costs and travel expenses, PCV20 was projected to generate savings in medical costs and societal costs compared with PCV15 over the 10-year time horizon.

Figure 1. DSA results: PCV20 versus PCV15

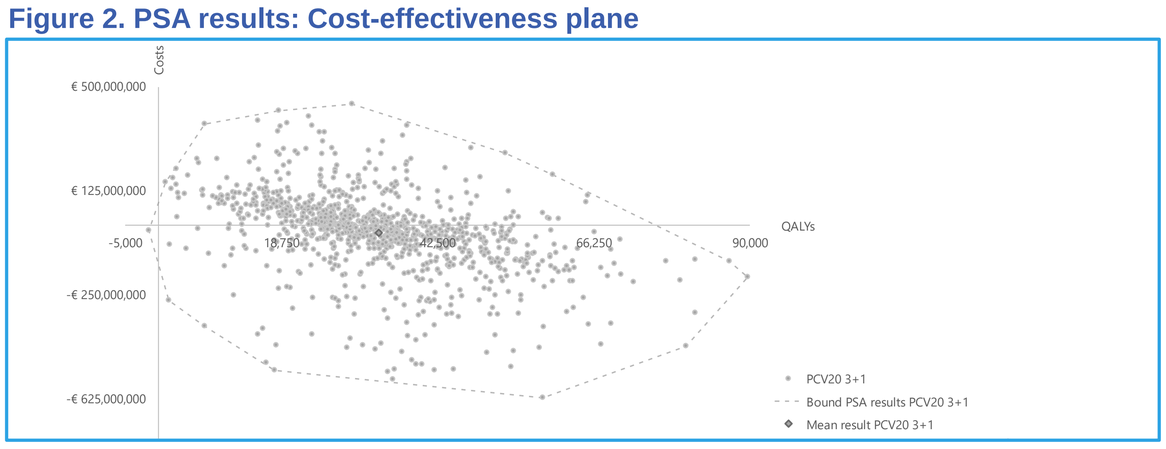


Abbreviations: DSA, deterministic sensitivity analysis; IPD, invasive pneumococcal disease; QALY, quality-adjusted life year; PCV, pneumococcal conjugate vaccine.

Sensitivity and scenario results

- The DSA identified the maximum indirect effect against hospitalized pneumonia from PCV20 as the primary driver of QALYs and costs (**Figure 1**).
- In the PSA, PCV20 was the dominant strategy compared with PCV15 in 57.0% of the 1,000 simulations, while being more effective but more costly in 42.9% of simulations (**Figure 2**).
- All tested scenarios confirmed PCV20 as the dominant or cost-effective strategy at a willingness-to-pay threshold of €20,000 per QALY.

Figure 2. PSA results: Cost-effectiveness plane



The PSA was assessed at a willingness-to-pay threshold of €20,000 per QALY per Zorginstituut Nederland Guidelines.[5] Abbreviations: PCV, pneumococcal conjugate vaccine; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life year.

CONCLUSIONS

This cost-effectiveness analysis demonstrated that implementation of PCV20 3+1 instead of PCV15 2+1 in the Dutch pediatric NIP would reduce the clinical burden of, and costs associated with, pneumococcal disease, making PCV20 the dominant vaccination strategy.

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