Health economic evaluation of replacing PCV13 with PCV15 in the Danish Childhood Vaccination Programme

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Objectives

Background

Pneumococcal disease is a major cause of morbidity and mortality worldwide, especially in children younger than five and elderly persons aged 65 and above. Since 2010, the 13-valent conjugated vaccine PCV13 has been part of the Danish Childhood Vaccination Programme (DCVP). MSD has developed a 15-valent pneumococcal conjugate vaccine, PCV15, which contains serotypes 22F and 33F in addition to the 13 serotypes included in PCV13.

Aim

The study aimed to estimate the health gains and the economic impact of replacing PCV13 with PCV15 in the DCVP.

Methods

Model structure

A Markov model was adapted to a Danish healthcare setting to simulate the incidence, costs and mortality of non-bacteraemic pneumococcal pneumonia (NBPP), invasive pneumococcal disease (IPD), acute otitis media (AOM) and post-meningitis sequelae (PMS) in the Danish population over a time horizon of 100 years.

Incidence of pneumococcal disease

- All individuals (including newborns) enter the model with no pneumococcal disease and are subsequently at risk of developing IPD, AOM or pneumonia. The age-specific incidence of pneumococcal disease is presented in **Table 1**. The incidence of IPD was based on Danish incidence data published by the ECDC[1] and was stratified into meningitis, bacteraemia without focus or bacteraemic pneumonia[2]
- The incidence and case fatality rate of all-cause pneumonia, ie, community-acquired pneumonia (CAP), for all age-groups were sourced from Søgaard et al. (2014)[3]. Similarly, the age-specific risk of AOM occurrence stratified by simple AOM and recurrent AOM for different age categories (until 19 years of age) were sourced from Edmondson-Jones et al. (2021)[4]

Table 1. Incidence of pneumococcal disease

Inputs	Age 0-1	Age 2-5	Age 6-19	Age 20-44	Age 45-64	Age 65-74	Age >75
IPD incidence per 100,000	11.34	4.18	1.36	0.95	12.65	47.22	47.22
Case fatality rate	14.77%						
NBPP incidence per 100,000	305	305	78	147	538	743	721
Case fatality rate	0.10%	0.10%	0.40%	1.20%	8.40%	14.30%	24.90%
AOM	9,441	3,886	4,358	-		-	-

Table 2. Serotype distribution

Input	Age group	PCV13	PCV15	Non-vaccine type
IPD and NBPP	Age 0-5	2.7%	12.2%	87.8%
	Age 6-64	12.9%	25.2%	74.8%
	Age > 64	9.6%	25.6%	74.4%
AOM	Age 0-5	42.9%	50.0%	50.0%

- The serotype specific vaccine efficacy (VE) are presented in **Figure 1**. A serotype-specific vaccine efficacy of 92% against IPD was applied for serotypes 22F and 33F in PCV15 as well as for the shared serotypes (except from serotype 3).[5] PCV15 has proven superior in the response to serotype 3 as compared to PCV13; hence, a differentiated VE was applied for IPD caused by serotype 3
- The VEs against all-cause pneumonia were based on results from the PCV10 clinical trials[6]
- The AOM VEs for PCV13 vaccine-type serotypes were based on efficacy estimates from the US,[7] whereas the VE PCV15 serotype VEs were assumed to be the same as the vaccine efficacy from the original PCV7 trial.[8] Finally, the VE for recurrent AOM with tube replacement was sourced from Black et al. (2000)[9]
- It was assumed that the vaccine efficacy was 100% of the initial protective efficacy during the first five years and decreased linearly to 0% over the next 10 years[10,11]
- The introduction of PCV7 and PCV13 in the DCVP led to significant reductions in the IPD incidence in adults caused by vaccine-type serotypes. Hence, it is expected that the introduction of PCV15 in the DCVP will cause a similar reduction in IPD incidence related to serotypes 22F and 33F as presented in **Table 3**. Based on data from Stoecker et al. (2013), a reduction of 7.8% per year was applied for the first five years after the introduction of PCV15[10]

Costs

- The analyses wereconducted according to established standards for cost-effectiveness analysis with a societal perspective in Denmark
- The societal perspective included the costs associated with productivity loss due to disease-related premature deaths, ie, IPD deaths and pneumonia deaths. It also includes travel costs associated with vaccine administration and with IPD, pneumonia, AOM and PMS-related disease manifestations. Key unit costs applied in the model are presented in **Table 3**

Table 3. Key economic inputs

Input		Cost (EUR)
Vaccination costs	Pneumovax® 0.5 ml vial	79.87[12]
	Prevnar® 0.5 ml vial	79.87
	Cost of administration	20.01[13]
Healthcare costs	Cost of IPD	3,790[14]
	Cost of NBPP	5,772[14,15]
	Cost of AOM	308[13,14]

Note: Healthcare costs are presented as the weighted average sum of direct and indirect healthcare costs across age categories and disease manifestations.

Results

- **Table 4** presents the incidence of pneumococcal disease and its associated mortality in the scenario where PCV13 remains recommended in the DCVP and in the scenario where PCV13 is replaced by PCV15. We find that an introduction of PCV15 in the DCVP prevents 655, 916 and 11,980 cases of IPD, NBPP and AOM, respectively, per 10,000 persons in a vaccination cohort over a 100-year time period. In addition, the introduction of PCV15 would prevent 95 deaths related to pneumococcal disease.
- **Table 5** presents the societal costs, including cost of lost productivity, for the two vaccination regimens by cost category over the time horizon of 100 years. We find that the total cost in the scenario where PCV15 is introduced in the DCVP is EUR 1,386 million, whereas the total cost in the scenario where PCV13 remains recommended in the DCVP is EUR 1,394 million. This implies an incremental saving of EUR 8.2 million (discounted) over a 100-year time period, with a vaccine coverage rate of 96.33%.

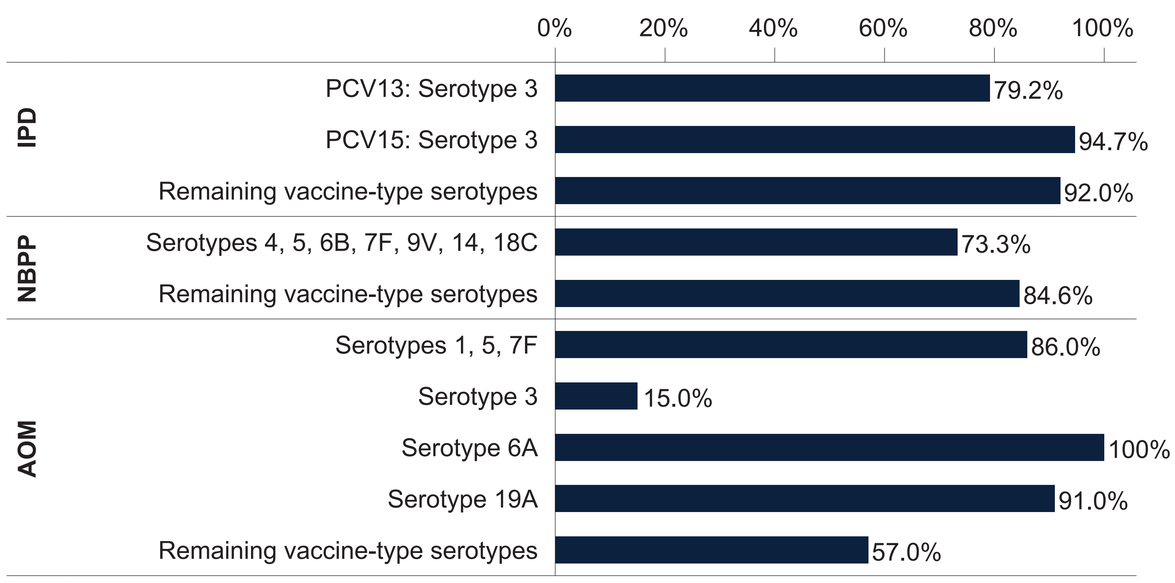
Table 4. Clinical outcomes

Clinical outcomes	PCV15	PCV13	Incremental cases
IPD cases	12,168	12,823	-655
Pneumonia cases	321,242	322,158	-916
AOM cases	913,141	925,121	-11,980
PMS cases	295	311	-16
IPD deaths	1,791	1,887	-96
Pneumonia deaths	13,568	13,567	1

Table 5. Societal costs by cost category

Cost categories	PCV15	PCV13	Incremental cost
Vaccine acquisition costs	66,066,185	66,066,185	0
Vaccine administration costs	16,554,298	16,554,298	0
IPD treatment costs	13,573,117	14,276,520	-703,403
Pneumonia treatment costs	608,726,728	610,328,772	-1,602,044
AOM treatment costs	74,071,232	74,966,708	-895,476
PMS treatment costs	1,867,883	1,959,622	-91,739
Indirect/non-medical costs	18,922,048	19,007,930	-85,882
Cost of premature death	586,246,920	591,089,783	-4,842,863
Total costs	1,386,028,413	1,394,249,819	-8,221,406

Figure 1. Vaccine efficacy



Conclusion

The findings suggest that replacement with PCV15 in the DCVP can prevent a significant number of pneumococcal cases and deaths and reduce pneumococcal disease-related costs.

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