

Public Health Impact of implementing a 20-valent pneumococcal conjugate vaccine in Turkish pediatric population

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INTRODUCTION

- Pneumococcal disease (PD), caused by *streptococcus pneumoniae*, is associated with over 100 serotypes, contributing to its significant global disease burden. [1]
- Turkey has a long history of using pneumococcal conjugate vaccination within National Immunization Program (NIP), starting in 2008 with PCV7, switching to PCV13 in 2011 and adopting 2+1 schedule in 2019 which lead to a significant reduction in PD cases. [2-5] Additionally, in 2016, adult vaccination with PCV13 was included. [6]
- However, even in countries with routine PCV vaccination, disease remains, especially disease due to serotypes not covered by currently implemented vaccines.
- The introduction of higher-valency PCVs would be expected to further reduce the burden of PD and prevent the emergence of PD caused by serotypes not covered by NIP standard of care.

OBJECTIVE

- The study aims to estimate the clinical and economic impact of replacing PCV13 with PCV20 in the pediatric NIP in Turkey.

METHODS

Model Overview

- A decision-analytic model was adapted to assess the health and economic impacts of switching from PCV13 to PCV20 in Turkish infants.
- Clinical impact was assessed by comparing the number of pneumococcal disease cases and deaths after implementing a pediatric NIP with PCV20 vs. PCV13. Specifically, it evaluated the differences in cases for Invasive PD (IPD), and non-invasive disease including all-cause hospitalized and non-hospitalized pneumonia (PNE), and otitis media that could be associated with *streptococcus pneumoniae*, along with deaths due to IPD and hospitalized PNE. (Table 3 and 4)
- The economic impact was estimated by comparing the direct and indirect medical costs associated with cases of IPD, hospitalized and non-hospitalized pneumonia and AOM between PCV20 and PCV13.(Table 3 and 4).
- Model inputs were sourced from publicly available data sources (Table 1):**
 - Age-specific epidemiologic inputs (incidence rates for invasive pneumococcal disease, non/hospitalized pneumonia, otitis media) were sourced from United States due to lack of active surveillance data in Turkey and similarity between vaccine implementation in US in terms of valency and schedules. [7]
 - IPD and hospitalized pneumonia carry a risk of death, and their respective case fatality rates (CFRs) were taken from published reports and literature. [8]
 - Direct and indirect medical costs were mainly derived from local reports [9-11] and all costs were inflated to 2024 values in Turkish Lira. [12] Indirect costs were measured using human capital approach capturing productivity losses due to illness.
 - Serotype distribution was extracted from a local study starting from 2015 representing 24 different centers located in all geographical regions of Turkey. [13, 14]
 - Direct vaccine effectiveness in the model was based on PCV13 effectiveness and PCV7 efficacy data. [15-18] The indirect vaccine effectiveness (herd effects) that assesses the impact on the unvaccinated populations was based on real-world impact studies. [19-22] We assumed all PCVs have the same direct and indirect effects. (Table 2)
 - Vaccination rate [4] : 95.3% coverage of PCV13 for the priming series and assuming similar coverage rates for PCV20. Booster dose coverage was assumed to be the same as priming series.
- Impact outcomes were stratified by age groups. For children younger than 5 years were grouped by 12-months intervals, while individuals 5 years and older were grouped into 5–17, 18–34, 35–49, 50–64, and ≥65 years.
- Time horizon was set to 10 years with an annual discount of 3% for both costs and benefits. At the start of each annual cycle, a new birth cohort would enter the model and get vaccinated.

Table 1: Key Inputs

	Age Group									
	<12 months	12-23 months	24-35 months	36-47 months	48-59 months	5 - 17 years	18 - 34 years	35 - 49 years	50 - 64 years	65+ years
	Population (in thousands) *									
	934.22	1,031.30	1,078.49	1,116.76	1,187.29	16,857.98	21,787.86	18,720.68	13,935.00	8,722.81
	Serotype Coverage, % [13, 14]									
PCV-13	43.50	43.50	43.50	43.50	43.50	40.00	60.60	60.60	60.60	62.50
PCV-20	52.20	52.20	52.20	52.20	52.20	57.10	70.30	70.30	70.30	78.10
	Disease incidence per 100,000 individuals [7]									
IPD	13.70	10.40	4.30	4.30	4.30	1.40	2.30	6.90	15.60	23.70
Hospitalized PNE	684.00	485.00	453.00	235.00	192.00	94.00	122.80	122.80	475.90	1,477.20
Non-hospitalized PNE	2,007.00	3,774.50	3,268.00	3,268.00	3,268.00	1,245.40	622.90	622.90	1,104.30	2,864.50
AOM	64,770.00	62,218.00	38,974.00	38,974.00	38,974.00	11,765.00	-	-	-	-
	Case fatality rates, % [8]									
IPD**	7.01	5.26	3.45	3.45	3.45	4.62	4.88	7.91	11.1	14.17
Hospitalized PNE	1.30	0.53	0.40	0.42	0.61	1.34	1.40	1.40	3.80	7.97
	Direct Medical Cost (per episode), ₺ [9-11]									
IPD	247,815.6	247,815.6	247,815.6	247,815.6	247,815.6	247,815.6	259,661.0	259,661.0	259,661.0	150,718.3
Hospitalized PNE	10,596.1	30,900.3	30,900.3	30,900.3	30,900.3	51,204.4	68,687.2	68,687.2	68,687.2	68,687.2
Non-hospitalized PNE	2,070.8	6,038.8	6,038.8	6,038.8	6,038.8	10,006.8	13,423.4	13,423.4	13,423.4	13,423.4
AOM	588.4	538.4	538.4	538.4	538.4	488.4	-	-	-	-
	Indirect Medical Cost (per episode), ₺ [9-11]									
IPD	62,247.7	62,247.7	62,247.7	62,247.7	62,247.7	70,070.6	70,070.6	70,070.6	70,070.6	70,070.6
Hospitalized PNE	7,574.3	11,189.8	11,189.8	11,189.8	11,189.8	14,805.3	8,547.4	8,547.4	8,547.4	-
Non-hospitalized PNE	1,623.9	2,399.1	2,399.1	2,399.1	2,399.1	3,174.2	1,084.6	1,084.6	1,084.6	-
AOM	2,757.5	2,757.5	2,757.5	2,757.5	2,757.5	2,757.5	-	-	-	-

*Population data was extracted from local reports. Proportion of IPD due to meningitis is 7%, and the proportion due to bacteremia is 93% [7] across all age groups.

Abbreviations: IPD, invasive pneumococcal disease; PNE, pneumonia; AOM, acute otitis media

**IPD includes both meningitis and bacteremia

Table 2: Vaccine Direct and Indirect effects assumptions

Model Assumptions for All PCVs	Base Case Data Assumptions	Base Case Values	Age Groups
Direct Effects			
IPD**	PCV13 real-world effectiveness data on vaccine-type pneumococcal disease [18]	88.7%	<2 years of age
All-cause hospitalized PNE	PCV7 clinical efficacy data on all-cause non-invasive disease [15-17]	25.5%	<2 years of age
All-cause non-hospitalized PNE		6.0%	
AOM		7.8%	
Indirect Effects			
IPD	PCV13 real impact data on pneumococcal disease [21]	83.0%	<18 years of age
		88.0%	18-49 years of age
		77.0%	50-64 years of age
		73.0%	65+ years of age
All-cause Hospitalized PNE	PCV13 real-world impact data on non-invasive data [19-22]	43.8%	<5 years of age
		35.6%	5-17 years of age
		22.5%	18-49 years of age
		25.2%	50-64 years of age
		26.9%	65+ years of age
		32.3%	<5 years of age
All-cause non-hospitalized PNE	26.2%	5-17 years of age	
AOM	28.0%	<18 years of age	

- Over 10 years, PCV20 was estimated to incrementally prevent 10,306 IPD cases, 229,885 pneumonia cases and ~1.4 million cases of AOM, and avert 7,097 deaths, which implies that the estimated overall **relative disease case and the death reductions would be 2.8% and 4.1%, respectively.**
- As a result, switching from PCV13 to PCV20 across all age groups led to an additional \$9.24 billion saved in direct medical costs and \$4.38 billion in indirect medical costs, which implies that the estimated **overall relative medical cost reduction would be 2.9%.**

Table 3: Clinical and economic impact of PCV20 vs. PCV13

	Estimated Disease Cases, Deaths, Direct and Indirect medical costs over 10 years with		Estimated disease impact (PCV20 vs. PCV13)
	PCV13	PCV20	
IPD	75,454	65,148	-10,306
Non-hospitalized pneumonia	11,132,815	11,015,424	-117,393
Hospitalized pneumonia	3,302,213	3,189,722	-112,492
AOM	43,671,482	42,271,627	-1,399,854
Deaths due to disease	174,383	167,288	-7,097
Estimated Total Direct Medical costs (Billion TRY)	335.4	326.2	-9.2
Estimated Total Indirect Medical costs (Billion TRY)	131.2	126.8	-4.4
Estimated Total Medical costs (Billion TRY)	466.6	453.0	-13.6

Table 4: Yearly averted cases, deaths and cost savings: PCV20 vs PCV13

	year 1	year 2	year 3	year 4	year 5	year 6	year 7	year 8	year 9	year 10
	IPD									
PCV 20 vs. PCV13	31	465	667	873	1,091	1,346	1,392	1,440	1,482	1,519
Non-hospitalized pneumonia										
PCV 20 vs. PCV13	325	6,223	8,618	10,894	13,121	15,774	15,746	15,675	15,589	15,428
Hospitalized pneumonia										
PCV 20 vs. PCV13	336	4,930	7,084	9,302	11,707	14,612	15,249	15,916	16,454	16,902
AOM										
PCV 20 vs. PCV13	9,664	76,010	103,788	130,061	155,371	185,269	185,542	185,356	185,003	183,790
Deaths due to disease										
PCV 20 vs. PCV13	5	286	424	568	727	921	971	1,025	1,067	1,103
Direct Costs, million TRY										
PCV 20 vs. PCV13	20.38	474.12	662.64	843.19	1,026.05	1,237.49	1,243.95	1,250.25	1,247.73	1,238.35
Indirect costs, million TRY										
PCV 20 vs. PCV13	31.77	264.00	352.13	431.32	504.08	587.21	574.08	560.11	545.92	529.77

CONCLUSIONS

- Replacing PCV13 with PCV20 in the Turkish pediatric NIP is estimated to avert more PD cases and deaths while saving greater medical costs over ten years.
- The earlier replacement with PCV20 could accelerate the clinical and economic impact

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