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Potential Cost-Effectiveness of Pneumococcal Conjugate Vaccine (PCV) in Turkey

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A B S T R A C T

Background: Pneumococcal infection is an important and preventable cause of morbidity and mortality. The Turkish government introduced 7-valent pneumococcal conjugate vaccine (PCV) into the national immunization program in 2009. This suggests that replacing 7-valent PCV with a higher-valent version could at least maintain "standard of care" if not improve it, and that it could be affordable. **Objectives and Methods:** The aim of this analysis was to assess the potential direct cost-effectiveness of 13-valent PCV in Turkey, a country with a birth cohort of 1.4 million, against a "no vaccine" state, against the default 7-valent PCV state, and against a 10-valent PCV state, using a published cohort model with a 5-year horizon. **Results and Conclusions:** The cost per life-year gained is below the 1 × per-capita gross domestic product threshold across large changes in key input parameters, indicating that the model is stable and suggesting that any PCV would be very cost-effective in a Turkish national pediatric immunization schedule.

Keywords: burden of disease, children, cost-effectiveness, pneumonia, vaccines.

Methods

The Model

Details of the model have been published previously [1]. The inputs are shown in Table 1 [2,4,6–10]. At all opportunities, we have erred toward a conservative utilization of the inputs. For comparison, UK inputs are also shown [1].

Burden of Disease

The epidemiological data used in the model are derived from a study of 12 Istanbul hospitals [2], which cover 65% of the overall Istanbul population of 13 million. This, in turn, represents 19% of the overall Turkish population of 70 million.

The annualized rate of pneumococcal meningitis in children younger than 5 years is between 3 and 5 per 100,000, for pneumococcal septicemia 7.5 to 22.5 per 100,000, for hospitalized (average 6 days) and community suspected pneumococcal pneumonia between 210 and 2790 per 100,000, for all-cause otitis media 330 per 1000, and for pneumococcal otitis media 58 per 1000.

Vaccine Efficacy

The efficacy of 7-valent pneumococcal conjugate vaccine (PCV) and of 13-valent PCV against invasive pneumococcal disease (IPD) was assumed to be at the lower end of the 95% confidence interval (83%) [4], for suspected pneumococcal pneumonia 20.5% [6], and for all-cause otitis media 6% [7]. The efficacy of 10-valent PCV against IPD was assumed to be at the lower end of the 95% confidence interval (83%) [5]. Its efficacy for suspected pneumococcal pneumonia was assumed to be 20.5% and for pneumococcal otitis media 41.4% [3]. While longer-term vaccine effectiveness for all indications was assumed to be of at least 5 years' duration [11], vaccine effectiveness was assumed to decrease at a rate of 2% every 6 months; by age 5 years, the effectiveness was assumed to have decreased by 18% [8].

Serotype Coverage and Serotype-Specific Efficacy

The serotype coverage for infants and children in Turkey for 13-valent PCV was taken to be 74%, for 10-valent PCV 61%, and for 7-valent PCV 38% [9]. The serotype-specific age-specific vaccine efficacy for IPD reduces to 26% at 60 months for 7-valent PCV, to 42% for 10-valent PCV, and to 51% for 13-valent PCV.

Herd Protection

Not incorporated.

Cost of Disease Treatment

All the disease treatment costs are local costs (converted to 2011 US$). Only direct costs were applied. The cost of treating a pediatric patient with pneumococcal bacteremia/septicemia was

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Table 1 – Model inputs.

	Input	Source
Incidence of meningitis per 100,000	4 (up to 2 mo) (UK = 11) [1] 5 (up to 24 mo) (UK = 5–200) [1] 3 (up to 60 mo) (UK = 20) [1]	Local data [2]
Incidence of bacteremia/ septicemia per 100,000	7.5 (up to 2 mo) (UK = 6.70) [1] 15 (up to 6 mo) (UK = 5.80) [1] 22.5 (up to 24 mo) (UK = 6–140) [1] 12.5 (up to 60 mo) (UK = 3.50) [1]	Local data [2]
Incidence of suspected pneumococcal pneumonia per 100,000	1,710 (up to 2 mo) (UK = 4500) [1] 2,790 (up to 6 mo) (UK = 880) [1] 2,290 (up to 12 mo) (UK = 15,000) [1] 1,320 (up to 24 mo) (UK = 1,300) [1] 210 (up to 60 mo) (UK = 890–1,970) [1]	Local data [2]
Incidence of all-cause otitis media per 1,000	330 (up to 60 mo) (UK = 23–62) [1]	Local data [2]
Incidence of pneumococcal otitis media per 1,000	58 (up to 60 mo)	Prymula et al. [3]
IPD vaccine efficacy	83% (7-valent PCV and 10-valent PCV) 83% (10-valent PCV)	Black et al. [4] Palmu et al. [5]
Vaccine efficacy against suspected pneumococcal pneumonia	20.5% (7-valent, 10-valent, and 13-valent PCV)	Black et al. [6]
All-cause otitis media vaccine efficacy	6% (7-valent PCV and 13-valent PCV)	Eskola et al. [7]
Pneumococcal otitis media vaccine efficacy	41.4% (10-valent PCV)	Prymula et al. 2006 [3]
Reduction in vaccine effectiveness over time	Decrease at a rate of 2% every 6 mo; reduced by 18% at 60 mo	Extrapolated from Heath et al. [8]
Serotype coverage	38% (7-valent), 61% (10-valent), 74% (13-valent)	Erdem and Sener [9]
Costs	In-hospital cost of treating meningitis US $1,000 (UK = US $7,628) [1] In-hospital cost of treating bacteremia/septicemia US $500 (UK = US $4,254) [1] In-hospital cost of treating suspected pneumococcal pneumonia US $40 (UK = US $497) [1] Cost of treating a case of otitis media US $30 (UK = US $118) [1] Following meningitis, cost of treating: • deafness US $9,696 (UK = US $96,960) [1] • focal neurological deficit US $2,4613 (UK = US $24,230) [1] • chronic seizures US $758 (UK = US $7,592) [1] Cost of a death US $160 (UK = US $17,600) [1]	National Burden of Disease Study [10] and Turel et al. [2]
Mortality	Average of 1,879 deaths per year (24 per 100,000 population younger than age 5 y) of which 1,855 pneumonia-related and 24 IPD-related	National Burden of Disease Study [10]

IPD, invasive pneumococcal disease; PCV, pneumococcal conjugate vaccine.

US $500 and for pneumococcal meningitis, US $1000 [2]. The cost of treating suspected pneumococcal pneumonia is made up of 7500 hospitalized cases at US $325 per case and 142,500 outpatient cases at US $25 to US $60, with an average of US $40.50 per case [2]. The average cost of treating a case of pediatric otitis media was US $30 [10].

Cost of Disease Sequelae

The long-term cost of treating deafness, focal neurological signs, and chronic seizures following pneumococcal meningitis, occurring at rates of 15.5% [12], 6% [13], and 7% [14] respectively, was taken as one tenth the cost of treating such sequelae in the United Kingdom [1] based on the relative per-capita gross domestic products (GDPs) of Turkey and the United Kingdom, and was on average US $1700 per child with long-term sequelae. The cost of a death was US $160.

Mortality

For pneumococcal meningitis, there would be 17 deaths in a total of 555 cases, giving a case-fatality rate of 3.4% for those up to 24 months of age and 2.5% thereafter. For pneumococcal bacteremia/septicemia, there would be 7 deaths in a total of 264 cases, giving a case-fatality rate of 2.6%. The number of deaths due to suspected pneumococcal pneumonia is derived from the 13,253 deaths due to all causes reported in Turkey in the 7.794 million infants and children younger than 5 years [15]. Of these deaths, 1855 (14%) are reported to be due to suspected pneumococcal pneumonia. There would be a total of 150,020 cases of suspected pneumococcal pneumonia, thus giving an average case-fatality rate of 1.2%. This is lower than the pneumococcal pneumonia case-fatality rate of 6% for the Eastern Mediterranean region as reported in the Pneumococcal Global Burden of Disease study [16]. There would be no deaths attributed to otitis media.

Table 2 – Results.

	Cases averted with 7-valent PCV	Cases averted with 10-valent PCV	Cases averted with 13-valent PCV	Cases occurring if no vaccine
Cases (n)				
Meningitis	124	199	241	552
Bacteremia or septicemia	549	882	1,070	2,333
Suspected pneumococcal pneumonia	21,278	21,278	21,278	149,506
All-cause otitis media	215,856	NA	215,856	5,070,068
Pneumococcal otitis media	NA	262,427	NA	902,562
Lives saved	286	297	303	
CLYG (US $)	7,109	6,784	6,696	
Components of the incremental cost-effectiveness ratio (ICER) (US $)				
Total vaccine-related costs	160 million	160 million	160 million	
Total disease-related costs (before vaccination)	143 million	31.5 million	143 million	
Total disease-related costs (with vaccination)	136 million	23.0 million	135.5 million	
Life-years gained	21,483	22,278	22,727	

CLYG, cost per life-year gained; NA, not applicable/available; PCV, pneumococcal conjugate vaccine.

Discounting

Future health care costs were discounted at a rate of 3%. Some models also discount future benefits [17]. We performed a sensitivity analysis with a 6% discounting of future benefits.

Vaccine Cost, Schedule, and Vaccination Coverage

The cost of each dose of vaccine was taken to be US $30 plus an administration cost of US $3.26 for each dose, in a four-dose schedule and with 86% vaccine coverage in the population.

Cost-Effectiveness

A calculation of the mean cost of managing cases was performed for a vaccinated and an unvaccinated population. The results were expressed as cost per life-year gained and compared against World Health organization cost-effectiveness thresholds of "very

Table 3 – Sensitivity analysis (US $).

Parameter	Change	10-valent PCV	13-valent PCV
Base case		6,784	6,696
"Worst case"	All changed to "least favorable"	40,939	35,306
Pneumonia efficacy	Decrease to 4.4%	23,583	22,197
Vaccine cost	Increase by 50%	9,982	9,874
Treatment costs	Decrease by 50%	6,980	6,866
Otitis media efficacy	Decrease 10-valent PCV efficacy to 6%	6,838	NA
	Decrease 13-valent PCV efficacy to 3%	NA	6,822
Discount benefits	Increase to 6%	7,419	6,952
Discount costs	Increase to 6%	6,810	6,718
Cases of meningitis	Decrease by 50%	6,866	6,790
Hospitalization rate for pneumonia	Increase to 7.5%	6,795	6,707
Hospitalization rate for pneumonia	Decrease to 2.5%	6,747	6,659
Cases of meningitis	Increase by 50%	6,704	6,602
Discount costs	Decrease to 0%	6,754	6,670
Incidence of bacteremia/ septicemia	Increase by 50%	6,027	6,402
Otitis media efficacy	Increase 10-valent PCV efficacy to 69.3% for pneumococcal OM	6,573	NA
	Increase 13-valent PCV efficacy to 9% for all-cause OM	NA	6,570
Treatment costs	Increase by 50%	6,587	6,526
Pneumonia efficacy	Increase to 34%	4,234	4,210
Vaccine cost	Decrease by 50%	3,586	3,517

NA, not applicable/available; OM, otitis media; PCV, pneumococcal conjugate vaccine.

cost-effective" being 1 × per-capita GDP (US $10,471 in Turkey) and "cost effective" being 3 × per-capita GDP [18].

Sensitivity Analysis

Given that the model is a cohort model and not a Monte Carlo simulation, we chose to perform a one-way sensitivity analysis rather than a probabilistic sensitivity analysis.

Results

The results are shown in Table 2. The base-case cost per life-year gained would be US $7109, US $6784, and US $6696 for 7-valent, 10-valent, and 13-valent PCV, respectively. The cost of a national immunization program using any of the vaccines would be US $160 million. Using the World Health organization threshold, the implementation of a universal state-funded pediatric vaccination program using any PCV in Turkey is very cost-effective.

Sensitivity Analysis

The sensitivity analysis is shown in Table 3. The vaccine efficacy against suspected pneumococcal pneumonia, based on that for the Northern California Kaiser Permanente study [6], has the greatest impact on the results. If the efficacy of the vaccine was only 4.4%, the lower end of the 95% confidence interval, then the vaccine would cease to be very cost-effective but would remain cost-effective. Increasing the vaccine cost by 50% (to US $45) still renders the vaccines very cost-effective. Changing all the parameters to the "least favorable" pushes the vaccines just beyond the cost-effectiveness threshold.

The cost per life-year gained is below the 1 × per-capita GDP thresholds across large changes in key input parameters, indicating that the model is stable and suggesting that any PCV would be very cost-effective in a Turkish national pediatric immunization schedule.

Discussion

The main finding of this analysis is that any PCV would appear to be a very cost-effective intervention in the context of a national pediatric immunization schedule in Turkey, even without accounting for the added benefits of herd protection and other indirect effects such as societal savings. The main strengths of the analysis reside in the inclusion of predominantly local data and the use of an internationally recognized cost-effectiveness yardstick.

There is an inherent weakness in the way the national figures are derived in the present analysis in that the 12 Istanbul hospitals may not be representative of hospitals in the wider country and small inaccuracies in data at the 12 hospitals can be magnified into larger inaccuracies at a national level. The inclusion of UK incidence rates and costs, as well as the sensitivity analysis, provides a degree of confidence that such inaccuracies, if they exist, do not affect the results in a fundamental way.

The rates of pneumococcal infection used in the present analysis are either comparable to or less than those calculated and recently published for the Eastern Mediterranean Region [16]. The consequences for the present study are that the results are likely to be more conservative than if a global estimate were to be used, and the results reflect what may be monitored in Turkey after the introduction of the vaccine.

For different regions of Turkey, the GINI coefficient, a measure of equality, suggests that within the different regions of Turkey there is inequality, but that the inequality is distributed evenly [19]. We believe that the Turkish national data on health care and the GINI coefficients provide a degree of confidence that our results are applicable to Turkey as an entity. Although it is difficult to compare cost-effectiveness across different therapeutic areas but using different measures, we have noted that the cost per disability-adjusted life-year in Turkey for the treatment of lung cancer is US $6141 and for hepatitis C treatment US $6638. Treatment for these conditions in Turkey is funded by the state.

A number of studies performed in countries with a socioeconomic background similar to that of Turkey also conclude that PCV would be cost-effective using direct medical costs (Colombia [20], Brazil [21], Taiwan [22], Malaysia [23], Argentina [24], and Uruguay [25]) or even cost-saving with the inclusion of societal costs (Mexico [26]).

In conclusion, it appears that any PCV, according to internationally accepted criteria, would be very cost-effective in a national Turkish pediatric immunization schedule.

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