Cost-utility analysis of new pneumococcal conjugate vaccines in the regional immunization program of the Autonomous Region of Madrid – Impact on invasive pneumococcal disease

Picazo J[1], Mendez C[2], Oyagüez I[3], Casado MA[3], Hwang S[4], Strutton D[4], Guijarro P[2]

[1] Medicine Faculty, University Complutense of Madrid, Spain; [2] Pfizer Spain,, Madrid, Spain; [3] Pharmacoeconomics and Outcomes Research Iberia, Madrid, Spain; [4] Pfizer Inc., Pennsylvania, United States.

International Society of Pharmacoeconomics and Outcomes Research (ISPOR) 13th Annual European Congress, 6-9 November 2010, Prague, Czech Republic.

BACKGROUND

- *Streptococcus pneumoniae* is a common gram-positive bacteria with more than 90 serotypes, which is often found in the nasopharynx of healthy individuals and can cause invasive pneumococcal disease (IPD), pneumonia and acute otitis media (AOM).
- Madrid Health authorities decided to introduce heptavalent pneumococcal conjugate vaccine (PCV7) in the routine immunization program in November 2006 (3+1 schedule; 2, 4, 6 + 18 months).[1-3]
- Newly, the EMA approved two new pneumococcal conjugate vaccines, 10-valent (PCV10) which covers three additional serotypes to PCV7 and 13-valent (PCV13) which includes six additional serotypes. Recently, a seamless transition to PCV13 has been recommended.
- The inclusion of the conjugate pneumococcal vaccine in the Madrid Region (MR) routine immunization program avoids cases, among others, of invasive pneumococcal disease caused by serotypes of *S.pneumoniae* contained in the vaccine.

OBJECTIVE

- The aim of the study is to assess the efficiency of conjugate pneumococcal vaccine – 13-valent (PCV13) versus 10-valent (PCV10), against IPD cases, under MR Healthcare System perspective.

METHODS

- A cost-utility model was developed to estimate cost per quality adjusted life year (QALY) associated to IPD (primary bacteriemia, empyema, meningitis and bacteriemic pneumonia) with vaccine administration in the Autonomous Region of Madrid.
- The model has been developed to assess the impact of systematic vaccination with the two new pneumococcal conjugate vaccines (PCV13 and PCV10) in the MR. (Figure 1)
- The model presents results over a 1-year time horizon.
- It considered a total population of 6,375,628 habitants in the MR[4] distributed in the following age groups: 0-2 years (2.4%), 2-4 (3.3%), 5-14 (11.7%), 15-34 (26.5%), 35-49 (25%), 50-64 (16.7%), ≥65 (14.4).
- The number of avoidable cases and serotype coverage was based on the HERACLES study[5-6] and epidemiologic information available at Regional level[7].
- Additionally to direct protection, the model considers the potential indirect effect on the general population[8].
- Results are expressed as incremental cost-utility ratio (ICUR) – relation between incremental costs (€) per quality-adjusted life years (QALY).

Schedule and vaccination coverage

- The vaccination schedule followed was 3+1 doses, the 2+1 schedule of PCV13[9] was also considered as an alternative in the sensitivity analysis.
- A vaccination coverage of 96% has been established for both vaccines[10].

Immunogenicity

- The magnitude of the immune response achieved by PCV10 was lower than that achieved by PCV7[11]. For this reason, we applied a correction factor of 94%, thus reducing the potential efficacy of PCV10 on direct and indirect effects[12].

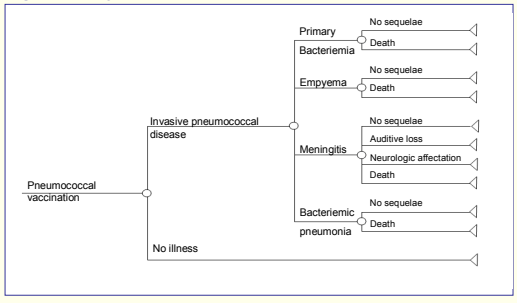
Costs estimation

- Only direct costs were considered (vaccine costs, administration costs and cost of diseases)[13-16].
  - Vaccination costs included the vaccine public ex-factory price (EFP) for one dose package[17].
- All cost are expressed in €2010
- An annual discount rate of 3% has been applied, following Spanish published recommendations[18].

Sensitivity analysis

- One-way sensitivity analyses were performed, including parameters with most uncertainty (Table 2).

Figure 1: Analytical decision tree



RESULTS

- PCV13 yields 224 QALYs versus 70 QALYs with PCV10. The incremental ratio is 16,908€/QALY gained. This results are showed in Table 2.

Table 2: ICUR of baseline model

	PCV13	PCV10	Difference
Total Costs (€)	14,953,869.67	12,353,869.48	2,600,000.19
Quality-adjusted life years	224	70	154
Cost/QALY (€) (PCV 13 vs PCV10)			**16,908.27 €**

- Deterministic sensitivity analysis showed that model results are robust, parameter that most influence on the results was vaccine indirect effect. Results of sensitivity analysis are shown in Table 3.
- Reducing PCV13 vaccine schedule from 4 to 3 doses is a dominant strategy.

Table 3: Sensitivity analysis results

PARAMETER		BC value	SA value	Incremental Cost (€)	Incremental QALYs	ICUR [Cost (€)/QALY]
BASELINE CASE				**2,600,000.19**	**154**	**16,908.27**
Discount rate		3%	0%	2,600,000.19	288	9,021.90
			5%	2,600,000.19	117	22,257.46
Vaccines indirect effect		not detailed	-10%	2,645,592.12	143	18,490.22
			-20%	2,689,784.38	133	20,275.10
Serotypes replacement	Direct effect		-10%	2,651,825.61	142	18,732.07
	Indirect effect		-10%			
	Direct effect		-10%	2,697,581.32	131	20,628.44
	Indirect effect		-20%			
	Direct effect		-20%	2,658,059.10	140	18,979.16
	Indirect effect		-10%			
	Direct effect		-20%	2,705,378.26	129	20,992.18
	Indirect effect		-20%			
Vaccination shedule PCV13	4 doses		3 dosis (Indirect effect PCV13 -19,8%)	-1,259,875.75	121	Dominant strategy
PCV10 immunogenicity	Direct effect		* 0,94	2,573,788.91	157	16,363.13
	Indirect effect		* 0,94			
Costs of diseases	Primary bacteriemia	4,093.46 €	3,684.11 € (-10%)	2,664,637.03	154	17,328.62
	Empyema	5,953.87 €	5,358.48 € (-10%)			
	Meningitis	11,201.84 €	10,081.66 € (-10%)			
	Bacteriemic pneumonia	5,420.40 €	4,878.36 € -10%)			
Price/dose vaccines		EFP dose-unit package	WAC dose -10 units package	2,278,301.30	154	14,816.21

BC: base case; SA: sensitivity analysis; ICUR: incremental cost-utility ratio; EFP: ex-factory price

CONCLUSIONS

- When considering the possible modification of a vaccination program, the efficacy, safety and disease prevention are such an important factors as its budget impact.
- Considering the efficiency threshold accepted in Spain, the results of the study (16,908€/QALY) suggest that PCV13 is a cost-effective alternative compared to PCV10.
- A 3 doses schedule of PCV13 is a dominant option, being a cost-saving strategy for the National Healthcare System.

REFERENCES

1. Kaplan SL, Barson WJ, Lin PL, Stovall SH, Bradley JS, Tan TQ, Hoffman JA, Givner LB, Mason EO Jr. Serotype 19A Is the Most Common Serotype Causing Invasive Pneumococcal Infections in Children. Pediatrics. 2010;125(3):429-36
2. WHO (World Health Organization). Pneumococcal Vaccines. Weekly epidemiological record 2003;78(14):97-120
3. Pineda Solas V. Vacunas conjugadas. Rev Pediatr Aten Primaria. 2005;7 Supl 4:S65-74 DD
4. Spanish National Institute of Statistics. Available at: http://www.ine.es
5. Picazo J, et al. Serotype –specific clinical outcomes of invasive pneumococcal disease in hospitalized pediatric patients in Madrid (May 2007-april 2008). Ped Infect Dis J. 2009;28:e71.
6. Picazo J, et al. Serotype distribution of invasive Streptococcus pneumoniae among hospitalized pediatric patients in Madrid (May 2007-april 2008). Ped Infect Dis J. 2009;28:e71 (P204).
7. Boletín Epidemiológico de la Comunidad de Madrid. Available at: http://www.madrid.org/cs/Satellite?c=PTSA_Multimedia_FA&cid=1142576838291&pagename=PortalSalud%2FPTSA_Multimedia_FA%2FPTSA_documentoWebedItpro.
8. Gonçalves G. Herd immunity: recent uses in vaccine assessment. Expert. Rev Vaccines. 2008;7:1493-506.
9. Prevenar® 13 Summary Product Information. Available at: http://www.ema.europa.eu/humandocs/PDFs/EPAR/Prevenar13/emea-combined-h1104es.pdf
10. Ministerio de Sanidad y Consumo. Salud Pública. Prevención y Promoción. Vacunaciones. Coberturas de vacunación. Available at: http://www.msc.es/profesionales/saludPublica/prevPromocion/vacunaciones/coberturas.htm#primero.
11. Synflorix® Summary Product Information. Available at:http://www.ema.europa.eu/humandocs/PDFs/EPAR/synflorix/emea-combined-h973es.pdf
12. Vesikari T, Wysocki J, Chevallier B, Karvonen A, Czajka H, Arsène JP, et al. Immunogenicity of the 10-valent pneumococcal non-typeable Haemophilus influenzae protein D conjugate vaccine (PHiD-CV) compared to the licensed 7vCRM vaccine. Pediatr Infect Dis J. 2009;28 Suppl 4:S66-76a.
13. Oblikue Consulting. Base de datos sanitarios e-salud. Available at: http://www. oblikue.com/bddcostes/
14. Cohen E, Weinstein M, Fisman DN. Cost-effectiveness of competing strategies for the treatment of pediatric empyema. Pediatrics. 2008;121:e1250-7.
15. Plans P. Coste-efectividad de la vacunación antineumocócica 23-valente en Cataluña. Gac Sanit. 2002;16:392-400.
16. Asensi F, De Jose M, Lorente M, Moraga F, Cluryla V, Arikian S, et al. A pharmacoeconomic evaluation of seven-valent pneumococcal conjugate vaccine in Spain. Value Health. 2004;7:36-51.
17. Ministry of Health and Social Policy. Interministerial Commission of prices 25th May 2010. Available at: http://www.msc.es/profesionales/farmacia/financiacion/home.htm
18. López Bastida et al. Propuesta de guía para la evaluación económica aplicada a las tecnologías sanitarias. Gac Sanit.2010; 24 :154-70