

Opportunities for Prevenar 13[®] vaccine in Campania region: a budget impact analysis

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ABSTRACT

BACKGROUND: Although the efficacy of pneumococcal vaccination for the more common serotypes of *Streptococcus pneumoniae* has been demonstrated, the 13-valent vaccine (Prevenar 13[®]) is still offered in different ways in the Italian regional healthcare units, and in the region of Campania, some local health authorities administer the vaccine free of charge whilst others practice a co-payment.

METHODS: We performed a budget impact analysis of the possible free administration of Prevenar 13[®] vaccine to all newborns in the Campania region, by comparing two different delivery settings, one having an active vaccination program and another in which such program was absent. During the operation of the vaccination program, the number of expected cases with 50, 80 and 100% vaccine coverage in the population was considered. The economic advantage resulting from pneumococcal diseases deemed avoidable thanks to the vaccination was compared with the costs of the vaccination program.

The analysis considered the direct costs in the 2 years after implementation of the vaccination program. Costs were expressed in € Euros 2010.

RESULTS: Although we did not consider the benefits achievable in the 10 years following the vaccination, nor the herd effects, we showed that offering anti-pneumococcal vaccination to all newborns could give economic advantages to the Region, estimated as close to 1 million Euros.

CONCLUSION: The use of Prevenar 13[®] can be considered a greatly advantageous public health strategy.

Key words: Pneumococcal diseases, Vaccination policies, Budget impact analysis, Conjugate vaccine

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INTRODUCTION

Pneumococcal diseases and vaccines

Pneumococcal diseases account for 1.6 million deaths each year, with 1 million of these occurring among children aged <5 years old (1). *Streptococcus pneumoniae* causes 10.6 million

infections in children annually (2). Pneumonia is the most common condition, with a higher incidence among children aged <2 years and adults aged >65 years; meningitis, sepsis and otitis media are also frequent, while sinusitis, endocarditis and peritonitis are rarely reported (3).

Resistance of pneumococci against antimicrobial drugs such as penicillin, cephalosporin and macrolides is increasing worldwide, and

in Italy, resistant strains account for 15–40% of isolates (4–6).

Currently, two types of vaccine are available: the pneumococcal polysaccharide vaccine (PPV), which contains purified capsular polysaccharides, and pneumococcal conjugate vaccines (PCVs), which are obtained through conjugation of the capsular polysaccharide to a carrier protein (7). PCVs elicit higher antibody levels than PPVs in infants and young children, and in the elderly and immuno-compromised persons, with a significant immunological memory resulting from subsequent booster doses. Moreover, PCVs reduce nasopharyngeal carriage of the pathogen, thus decreasing its circulation in the community and generating herd immunity (8).

The first PCV, Prevenar[®], contains poly- or oligosaccharides from seven *S. pneumoniae* serotypes (4, 6B, 9V, 14, 18C, 19F and 23F), each conjugated to genetically detoxified diphtheria toxin CRM 197. Its use was approved by the European Medicines Agency on February 2nd, 2001 (9).

Four large clinical studies of a heptavalent vaccine have reported an efficacy of 77–97% against invasive diseases caused by vaccine serotypes and an efficacy of 19–37% against pneumonia (10–13). The efficacy against otitis media was 57% (14). In Italy, a follow-up study on 70 000 children in the Liguria region estimated a 36.4% reduction in hospitalization for otitis media and a 70.5% reduction for pneumococcal pneumonia (15). A recent meta-analysis has shown an 80% efficacy against invasive diseases caused by vaccine serotypes and a 45–60% efficacy against those sustained by all serotypes (16). That study, included in the HTA report by La Torre et al. (17), confirmed the findings of a previous meta-analysis by Pavia et al. (18).

The effectiveness of the heptavalent vaccine has been partly reduced by an increased circulation of serotypes that are not included in the vaccine; in particular, serotypes 19A, 3 and 7F, which are contained in the new 13-valent formula (PCV13) (19, 20). This vaccine comprises the capsular polysaccharides of the 1, 3, 5, 6A, 7F and 19A serotypes, in addition to those contained in the heptavalent formula. The new antigens characterize serotypes that account for emerging infections, in particular the 1, 3 and 19A serotypes, which cause invasive diseases and often show antimicrobial resistance. On the basis of data available for Italy (21, 22), the conjugate 13-valent vaccine could increase serotype coverage by 45% more than the heptavalent vaccine.

Vaccine offer and economic evaluation

In Italy, vaccinations are planned and regulated by the National Vaccine Plan, which is discussed every 3 years and approved by the State-Regions Conference (23). Vaccination policies are monitored by an information system that assures the prompt collection of data about the efficacy of vaccination and adverse events (24). However, organization levels of the vaccine registers in our country are diverse: only 70% of local health authorities have computerized registers, while the remaining 30%, which are mainly represented by southern regions, lack computerization. The opportunity to improve the efficiency of vaccine services is related to two preliminary conditions: a) adequate training of, and the provision of information to, health personnel, and b) computerized inventories of vaccination registers in all the centers. Fair distribution of resources, which involves the rationalization of the health expenses incurred, is also an area of concern for the implementation of any good vaccination program. The recent debate about pneumococcal vaccination is a good example.

Pneumococcal vaccination provided a good opportunity to reorganize the whole system of vaccination policies in the various health authorities throughout the country, in an attempt to improve the efficiency of vaccine delivery (25). In the past few years, the anti-pneumococcal vaccine Prevenar[®] has been the most widely used conjugate vaccine in some settings (26). The need to increase serotype coverage has led to the preparation of an efficacious vaccine that contains 6 additional serotypes (Prevenar 13[®]). On December 9th 2009, the European Commission authorized the use of the pneumococcal conjugated vaccine, Prevenar 13[®] for active immunization against *S. pneumoniae* in children aged 6 weeks to 5 years. Subsequently, the Italian Medicines Agency (Agenzia Italiana del Farmaco; AIFA), on April 16th 2010, determined the reimbursement regime and the costs of the vaccine. Currently, 24 European countries have introduced Prevenar 13[®] into their vaccination programs (24). Anti-pneumococcal vaccination is still offered in different ways by the Italian regions, and in Campania, some local health authorities administer the vaccine free of charge to the entire pediatric population, while others offer it to high-risk groups only (Table 1) (26).

The situation in Campania has resulted from the recent solvency plans and, therefore, from choices that often correspond neither to the epidemiological reality nor to the social settings of the region. In 2004, with the decision n.1572, the Regional Council approved the Vaccinations Plan, which included pneumococcal vaccination. As for child immunization, the main target was represented by two cohorts: children aged <5 years, which presented social risk (Rom included) and children aged <36 months who attended a nursery (27). The Campania Health Department, with the letter n.2661/SP of June 15, 2006 (6), confirmed the need to offer this

The local health authorities in the Campania region behaved in different ways: Naples 1 Central, 2 North and 3 South, and Benevento currently offer the vaccine free of charge, while Caserta, Avellino and Salerno set a co-payment. Therefore, the need to carry out an economic evaluation of the implementation of an active and free vaccination strategy in the whole region became concrete.

The aim of the study was to carry out a budget impact analysis, in order to evaluate if the free offer of pneumococcal vaccination could reduce otitis, pneumonia and meningitis to the extent that it produces a positive economic effect for regional coffers.

TABLE 1

CURRENT OFFER OF PREVENAR 13 [®] IN ITALIAN REGIONS	
Region	Prevenar 13 [®] offer
Abruzzo	Free for infants in communities and co-payment for the others
Basilicata	Free and active
Calabria	Free and active
Campania	Active offer in 4 local health agencies and co-payment in the other 3
Emilia-Romagna	Free and active
Friuli-Venezia Giulia	Free and active
Lazio	Free and active
Liguria	Free and active
Lombardia	Free but not active
Marche	Free and active
Molise	Free and active
Piemonte	Free and active
Puglia	Free and active
Sardegna	Free and active
Sicilia	Free and active
Toscana	Free and active
Trentino-Alto Adige	Free and active
Umbria	Free and active
Valle d'Aosta	Free and active
Veneto	Free and active

vaccination actively and free of charge to the above-mentioned groups, and extended this to the pediatric population aged <5 years with a clinical risk for other diseases (28).

METHODS

The budget impact analysis was performed on the basis of the model proposed by Berto et al. (29), adapted to the newborn cohort of the Campania region (59 696 children in 2009).

We started from the incidence of pneumococcal otitis, meningitis and pneumonia in settings where a vaccination program was either present or absent, in reference to the study by Esposito et al. and by Pavia et al. (Table 2) (18, 30).

Therefore, the cost of each single case, as obtained from the studies by Lucioni et al., Giorgi-Rossi et al., Colombo and particularly by Berto et al. (28, 30-32) (Table 3), was multiplied by the number of events estimated in the two settings (absence or presence of a vaccination program). The difference between the relative costs represented the possible economic advantage for the Regional Health Service (RHS).

Subsequently, the cost of a single immuniza-

TABLE 2

	NUMBER OF CASES (%) OF PNEUMOCOCCAL DISEASES ESTIMATED IN PRESENCE OR ABSENCE OF A VACCINATION PROGRAM	
	Estimated cases	
	With vaccination	Without vaccination
	n (%)	n (%)
Otitis	23 878 (40%)	29 848 (50%)
Pneumonia	896 (1.5%)	2 985 (5%)
Meningitis	3 (0.05%)	59 (0.1%)
Total cases *	24 777	32 892

* 59 696 children

TABLE 3

COSTS OF ANTIPNEUMOCOCCAL VACCINATION AND PNEUMOCOCCAL DISEASES		
Costs	Amount (€)	Reference
Vaccine dose	42.58	Price to the LHA
Health worker	4.12	Italian Statistics National Institute (ISTAT)
Immunization	140*	Estimated values
Otitis:	30.59	Lucioni et al., 1999 Cost price
– Pediatric visit	18.54	
– Clavulanic Acid+Amoxicilline	12.05	
Pneumonia:	1 868.54	ISTAT Diagnosis Related Group (DRG) Campania
– Medical visit	18.54	
– Hospitalization	1 850	
Meningitis	10 696	Lucioni et al., 1999

tion (price of a dose for the Local Health Authority (LHA) + health worker fee per hour) and that of the entire vaccination program was calculated (Table 3). The analysis considered the perspective of the National Health Service (NHS) only (direct costs in €Euros 2010) for a period of 2 years from the start of the vaccination program. The possible economic advantage achievable through active vaccination with Prevenar 13® to all newborns in the Campania region, or that obtainable with 50 and 80% coverage, was calculated from the difference between costs for considered pneumococcal diseases and direct costs of vaccination, for each of the two years under consideration.

TABLE 4

COSTS (EXPRESSED IN € EUROS 2010) OF PNEUMOCOCCAL DISEASES WITH AND WITHOUT FREE ACTIVE VACCINATION OFFER							
	Unit	Costs (€)				Total costs for two years (€)	
		First year		Second year			
		With vaccination	Without vaccination	With vaccination	Without vaccination		
Vaccination	140.10	8 363 410	/	/	/	8 363 410	
Incidence	Otitis	30.59	730 428.02	913 050.32	730 428.02	913 050.32	365 244.60
	Pneumonia	1 868.54	1 674 211.84	5 577 218.19	1 674 211.84	5 577 218.19	7 806 012.70
	Meningitis	10 696.59	32 089.77	631 064.00	32 089.77	631 064.00	1 197 948.46
Economic advantage obtainable (€)		1 005 796.00					

*59 696 children

RESULTS

As shown by recent studies (17, 18, 30), the active offer of pneumococcal vaccination could appreciably decrease otitis, meningitis and pneumonia cases and relative costs (Table 4). The implementation of a free active offer of anti-pneumococcal vaccine could determine a reduction of costs in the two years considered, depending on the coverage level pursued. We hypothesized three different settings.

In the first case, by hypothesizing a vaccination strategy for all the 59 696 newborns of the reference year, the Campania Region would sustain a cost equal to € 8 363 410 for the vaccination program alone for two years. At the end of the two years considered, the immunization program could lead to a reduced incidence of pneumococcal diseases and consequently to a decrease in costs sustained for the treatment of these diseases, by producing a global economic advantage of almost a million Euros (Table 4).

In the second case, we considered a setting with an 80% coverage level, with a possible consequent rate of return equal to 804 635 at the end of two years (Table 5).

The last hypothesized setting was that of a 50% coverage level: in this case it could be possible to obtain a rate of return equal to € 502 897 after two years (Table 5).

DISCUSSION

The usefulness of pneumococcal vaccination in the pediatric population is supported by clinical and economic evidence, in addition

TABLE 5

ECONOMIC ADVANTAGE ACHIEVABLE WITH A FREE ACTIVE OFFER OF THE 13-VALENT PNEUMOCOCCAL VACCINE AT 80% OR 50% COVERAGE LEVELS				
Vaccination coverages	Vaccinated subjects (n.)	Immunization global cost (€)	Avoidable cases cost (€)	Economic advantage obtainable (€)
80%	47 756	6 690 728	7 495 363	804 635.00
50%	29 848	4 181 705	4 684 602	502 897.00

to the various positive implications associated with its ethical, organizational and efficaciousness aspects.

HTA evaluations represent the best analysis method to meet the expenses rationalization criteria, while adhering to the goals of public health (34, 35). Cost-effectiveness studies in Italy, which have considered direct and indirect effects, have supported the implementation of pneumococcal vaccination programs in many regions of the country (36). The inclusion of indirect effects in analytical and decision-making models improves the results obtained in favor of the adoption of vaccination programs substantially, with a consequent marginal cost-effectiveness ratio that attains good convenience values and global savings (37).

The introduction of pneumococcal vaccination in the Campania region could be a chance to reorganize the whole system of vaccination policies through new interventions that should improve the overall efficacy of vaccination. As for the organization of such a challenge, the personnel responsible for vaccination services should be adequately trained and vaccination centers should be computerized in order to increase the efficiency of the service. In fact, the rapidity and completeness of vaccination programs are fundamental for the relationship between information about vaccination and infectious diseases. Furthermore, to improve healthcare quality, training and information should involve the entire population, by giving the users a sense of responsibility (38). The distinction between mandatory and recommended vaccinations, which seems to underline the importance and efficacy of compulsory vaccines, significantly reduces compliance compared with other vaccines. This can influence the results of the programs, both from cultural and operational points of view.

On the basis of these elements, and con-

sidering the scarcity of epidemiological data, we tried to analyze the economic advantages of an active, free, pneumococcal pediatric vaccination program with Prevenar 13[®] in the Campania region.

The results of the present study confirm, for Campania, that which has also been shown at a European and Italian level. In essence, expenses sustained for the vaccination program with Prevenar 13[®] could be considerably balanced by the costs avoided for the treatment of pneumococcal diseases. It should be noted that the present study analyzed direct costs only. Although indirect costs were not considered, the adoption of a vaccination strategy with Prevenar 13[®] revealed itself to be economically advantageous even with a coverage level of 80 or 50% of the pediatric population. Other expenses for citizens, such as those for possible private medical visit or medicines which are not reimbursable, should also be considered. Indirect costs that are represented by loss in productivity (i.e. absence from work of parents), social costs linked to activities carried out in the community, or intangible costs could also be considered. Therefore, any judgment about the economic implications of vaccination could be strengthened if one considers these costs also.

Although it was incomplete, this perspective analysis suggests that the advantages could also be underestimated because we did not consider either the possible advantages obtainable at least for ten years or the indirect effect of herd immunity.

It is possible to affirm that pneumococcal vaccination represents a public health winning strategy because the new vaccine is more efficacious and could give economic advantages to the Region coffers. The adoption of Prevenar 13[®] could be thus considered a health policy which is both economically and clinically convenient.

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