

USE OF SEVEN-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV7) IN EUROPE, 2001-2007

H De Carvalho Gomes (Helena.Gomes@ecdc.europa.eu)¹, M Muscat², D L Monnet¹, J Giesecke¹, P L Lopalco¹

1. Scientific Advice Unit, European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

2. EUVAC.NET hub, Department of Epidemiology, Statens Serum Institut, Copenhagen, Denmark

The first pneumococcal vaccine targeting the youngest age groups, a seven-valent conjugate vaccine (PCV7), was licensed in Europe in 2001. Since then several European countries have introduced PCV7 in their childhood vaccination schedules. Still, information on vaccination schemes, vaccine uptake and impact of vaccine introduction is scarce in Europe. The following article summarises the characteristics of national pneumococcal vaccination programmes for children in 32 European countries and provides an estimate of vaccine use based on sales data for 22 countries between 2001 and 2007. There were wide variations in the recommended PCV7 vaccination schemes and in PCV7 use. High vaccine uptake was not always related to the presence of a national vaccination programme.

Introduction

Pneumococcal infection is an important cause of otitis media, pneumonia, septicaemia and meningitis leading to significant morbidity and mortality, particularly in young children and elderly people. The first vaccine targeting children, a seven-valent pneumococcal conjugate vaccine (PCV7), was first licensed in the United States in 2000 [1] and vaccination coverage has since increased from 89% (≥ 1 dose PCV7) and 68% (≥ 3 doses PCV7) among children born in 2001 to 95% and 84%, respectively, among children born in 2005 [2].

Following the European Union (EU)'s authorisation in 2001 for PCV7 use in children aged between the age of two months and five years [3], European countries have gradually introduced PCV7 in their vaccination schedules. In contrast to the situation in United States, there is little data on PCV7 vaccination coverage in European countries. This article provides an overview of the current national pneumococcal vaccination programmes in children and uses country-specific sales data to provide an estimate of PCV7 use in European countries.

Material and methods

Information about current national pneumococcal vaccination programmes for children in 32 European countries, including all 27 EU countries plus Croatia, Iceland, Norway, Switzerland and Turkey, was submitted by the national public health or surveillance institutions to the European surveillance network for vaccine-preventable diseases (EUVAC.NET) hub (see Acknowledgments). Data were collected between March 2008 and March 2009.

The only PCV7 licensed so far in the EU is a vaccine covering *Streptococcus pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F and 23F, conjugated to the CRM197 carrier protein and adsorbed on 0.5 mg of aluminium phosphate (Prevenar™, Wyeth). Annual PCV7 sales data in 22 European countries for this period were provided by Wyeth, the marketing authorisation holder and manufacturer of the vaccine. For each country, population data by age group were obtained from the online database of Eurostat, the statistical office of the European Communities [4]. PCV7 use was estimated by calculating (a) the yearly rate of PCV7 doses sold per 100 live births between 2001 and 2007, and (b) the cumulative number of completed vaccination courses (based on either three or four doses, according to the national schedules) per 100 live births for the period from 2005 to 2007. The yearly number of live births (birth cohort) was used as the denominator for all countries, including those that recommend vaccinating risk groups, as data on the size of the different risk groups was not available.

Results

National PCV7 vaccination programmes

By January 2009, 24 (75%) of the 32 participating European countries had introduced or decided to introduce vaccination against pneumococcal disease in their childhood vaccination schedule (see Table). Seven (29%) of these schedules offer PCV7 to risk groups only. In Italy, either risk-based or universal vaccination programmes are used, depending on the region. Twenty (83%) of 24 countries with a vaccination programme against pneumococcal disease started the programme in 2005 or later. Twelve (50%) countries recommend a 3+1 dose vaccination regimen and 11 countries recommend a 2+1 regimen. Switzerland uses a 3+1 regimen for risk groups and a 2+1 regimen for other children.

There is some variation regarding reimbursement of the vaccine. However, most of the countries (92%, n=22) with an established programme offer the vaccine free of charge or at least offer cost sharing for the respective target group. In Italy, the reimbursement policy (full reimbursement versus cost-sharing) varies depending on the region. Among countries with universal vaccination programmes, 11 have implemented catch-up programmes with different schemes.

PCV7 use

In almost all countries, and especially in the countries that have already introduced PCV7 in their childhood vaccination schedule,

TABLE

Characteristics of national pneumococcal vaccination programmes for children in 32 European countries

Country	Extent of PCV7 vaccination programme	Date of implementation	Vaccination regimen	Catch-up programme	Reimbursement	Comments
Austria	Universal	September 2004	3+1	No	No	Free of charge for children under the age of two years in risk groups.
Belgium	Universal	January 2005	2+1	Yes ^b	Total	Free of charge for children under the age of two years since January 2007
Bulgaria	None	-	-	-	-	Inclusion of PCV7 as a recommended vaccine on an individual voluntary basis is being considered based on a decision of the expert committee on national immunisations (24 July 2008).
Croatia	Risk-based	November 2006	3+1	n/a	Total	Since August 2008 free of charge for children at the ages of two, four and six months, with a booster dose at the age of 12-15 months (3+1). In addition, a catch-up programme is implemented for children up to the age of 59 months.
Cyprus	Universal	August 2008	3+1	Yes	Total	
Czech Republic	Risk-based	January 2007	3+1	n/a	Total	Free of charge for children under the age of five years since January 2007.
Denmark	Universal	October 2007	2+1	Yes ^c	Total	
Estonia	None	-	-	-	-	
Finland	Risk-based	January 2009	2+1	n/a	Total	Since January 2009, free of charge for children under the age of five years in risk groups. In addition, one dose of pneumococcal polysaccharide vaccine is given to children over the age of two years in risk groups.
France	Universal	June 2006	2+1	Yes ^d	Cost sharing/total	In October 2008, the vaccination regimen changed from 3+1 to 2+1. 65% of the price of PCV7 is reimbursed by social security. The rest is reimbursed by private insurance (for the 80% of the population that have one). The vaccine is free of charge in mother and child care services.
Germany	Universal	July 2006	3+1	Yes ^e	Total	Since January 2008, reimbursement of all recommended vaccinations has been regulated on a national level.
Greece	Universal	March 2006	3+1	Yes ^b	Total	Fully reimbursed since March 2008
Hungary	Universal	October 2008	3+1	Yes ^b	Total	Since October 2008, PCV7 has been given on a voluntary basis and free of charge to children under the age of two years with the 3+1 regimen. As of April 2009, PCV7 will be given free of charge to children at the age of two and four months, with a booster dose at the age of 15 months (2+1 regimen).
Iceland	Risk-based	December 2006	2+1	n/a	No	
Ireland	Universal	September 2008	2+1	n/a	Total	Free of charge for all children.
Italy	Universal/ risk-based	May 2005	2+1	No	Cost sharing/total (regional variation)	In 15 of 20 regions, PCV7 is offered to all children either free of charge or with cost sharing. In five regions, PCV7 is recommended to children at risk only and is free of charge.

Latvia	None	-	-	-	-	-	Voluntary vaccination of children in risk-groups is planned for 2009.
Lithuania	None	-	-	-	-	-	
Luxembourg	Universal	October 2004	3+1	Yes ^d	Total		
Malta	Risk-based	January 2007	3+1	n/a	Total		
The Netherlands	Universal	June 2006	3+1	-	Total		
Norway	Universal	July 2006	2+1	Yes	Total		PCV7 was introduced in the national childhood vaccination programme on 1 July 2006, with a catch-up programme for children born after 1 January 2006.
Poland	None	-	-	-	-	-	
Portugal	None	-	-	-	-	-	The Portuguese National Vaccination Committee is in the process of discussing the implementation of PCV7 into the national vaccination programme.
Romania	None	-	-	-	-	-	
Slovakia	Universal	April 2008	2+1	n/a	Cost sharing		Universal: recommended to children under the age of two years as complementary (optional) vaccination for optimal individual protection. 96% of the costs are reimbursed by the national health insurance.
	Risk-based	January 2006	2+1		Total		Free of charge to children under the age of two years belonging to risk groups.
Slovenia	Risk-based	September 2005	3+1	n/a	Total		Fully reimbursed since September 2005.
	Risk-based	June 2001	3+1	n/a	Total		Free of charge for children under the age of five years since June 2001.
Sweden	Universal	January 2009	2+1	n/a	Total		Since January 2009, PCV7 has been part of the national childhood vaccination programme and is recommended to all children born from October 2008 onwards.
	Universal	November 2005	2+1	Yes ^d	Total		Universal: recommended as complementary (optional) vaccination for optimal individual protection; fully reimbursed since August 2006.
Switzerland	Risk-based	July 2001	3+1				Risk-based: fully reimbursed since July 2001.
	None	-	-	-	-	-	
Turkey	Universal	September 2006	2+1	Yes ^b	Total		Free to all children

n/a = not applicable

a Number of PCV7 doses given during first year + number of booster doses

b Until 23 months of age for all children

c Until 18 months of age for all children

d Until 23 months of age for all children and until 59 months of age for children with particular co-morbidities

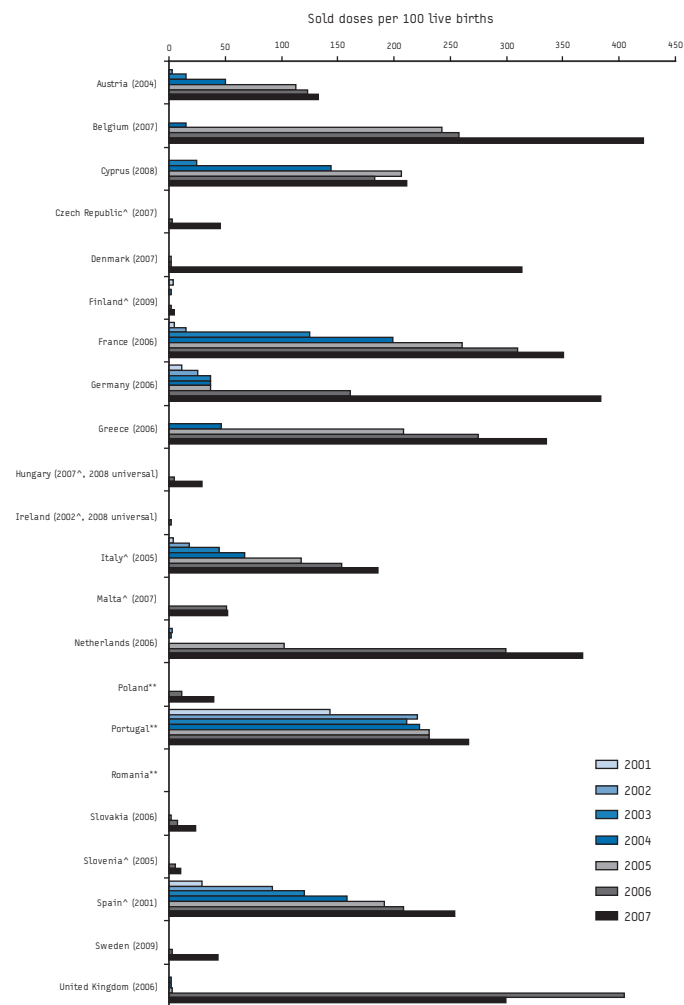
e Until 59 months of age for children with particular co-morbidities

Source: EUVAC.NET

PCV7 sales increased in the period from 2001 to 2007 (Figure 1). An increasing trend in PCV7 sales could be observed in nearly all countries and the increase in PCV7 sales was especially marked in the year the childhood pneumococcal vaccination programme started or shortly thereafter.

The highest PCV7 use was registered in Belgium in 2007 (422 doses per 100 live births), followed by the United Kingdom in 2006 (405 doses per 100 live births). In both cases, the peak coincided with the introduction of PCV7 in the childhood vaccination schedule. An estimate of the cumulative number of complete PCV7 courses per 100 live births for each country in 2005-2007 is presented in Figure 2.

FIGURE 1
Sold PCV7 doses per 100 live births in 22 EU countries, 2001-2007

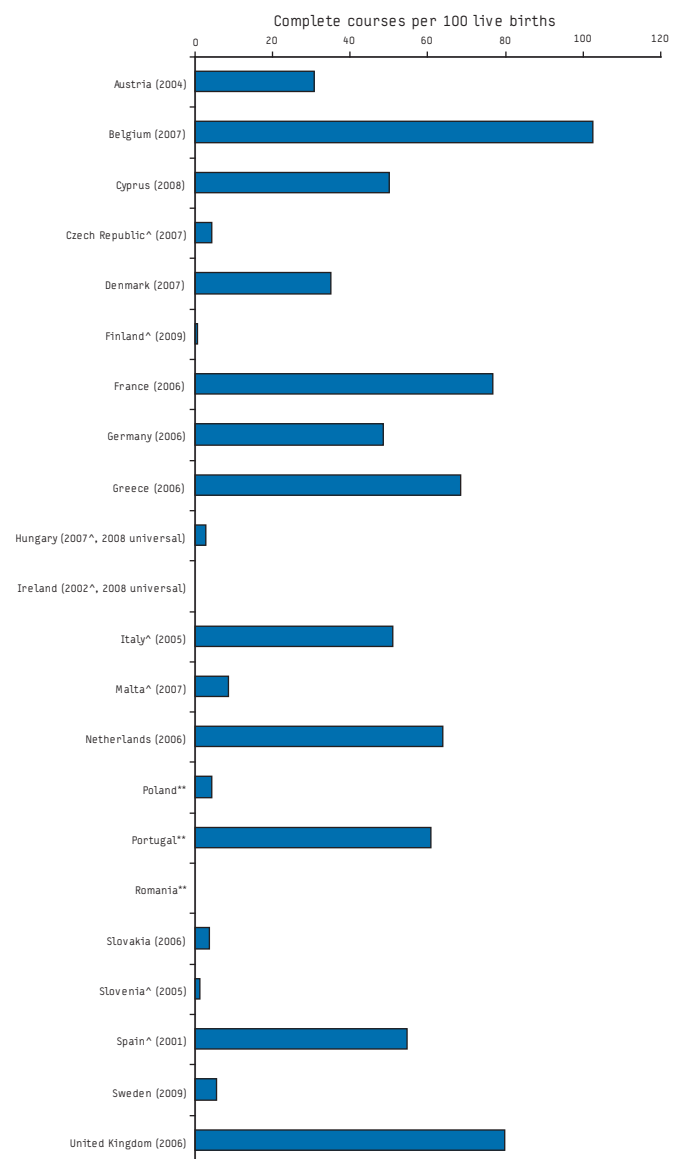


The data are shown as yearly sold doses per 100 live births in the respective year for 22 EU countries, for which sales data were available. For each country, the year of PCV7 introduction into the childhood vaccination schedule is shown in parenthesis.
 ^ Country with risk group programme only. Italy has a mix of universal and risk group programmes depending on the region.
 ** Country without childhood programme for vaccination against pneumococcal disease.

Discussion

This study presents the latest information on current national pneumococcal vaccination programmes in children in European countries. It also presents information on PCV7 use in the years from 2001 to 2007, based on sales data provided by the only PCV7 manufacturer in Europe during that time period. At the time of a previous review of PCV7 vaccination programmes in 2006, 19 European countries had recommendations for pneumococcal

FIGURE 2
Estimated number of complete PCV7 courses per 100 live births in 22 EU countries, 2005-2007



The cumulative number of complete PCV7 courses was estimated based on either three or four doses, according to the national schedules. For each country, the year of PCV7 introduction into the childhood vaccination schedule is shown in parenthesis.
 ^ Country with risk group programme only. Italy has a mix of universal and risk group programmes depending on the region.
 ** Country without childhood programme for vaccination against pneumococcal disease.

vaccination in children [5]. Among these, 10 had started a universal childhood pneumococcal vaccination programme. Three years later, seven additional European countries have introduced a universal pneumococcal vaccination programme for children. Although progress has been made to introduce PCV7 globally, only few countries outside Europe have introduced this vaccine into their national immunisation programmes for all children, and these are primarily high-income countries, i.e. the United States, Canada, Australia and New Zealand [6].

In each European country, the decision to introduce a new vaccine in the vaccination schedule is the result of careful discussions. In the case of PCV7, budget constraints have often been the principal driver in the decision-making process, especially in lower income European countries. PCV7 is an expensive vaccine to be proposed for childhood vaccination. Although the vaccine has been shown to decrease the incidence of invasive pneumococcal disease and pneumococcal pneumonia in children [7-11], different methods have been used to evaluate its cost-effectiveness and uncertainty remains as to whether a universal PCV7 vaccination programme in children would be cost-effective [12]. In the absence of adequate surveillance data, there have been concerns that the available vaccine may not cover all circulating pneumococcal strains. There have also been concerns about possible replacement of serotypes used in PCV7 by serotypes not covered by the vaccine [13,14]. As a consequence, the recommendations for PCV7 vaccination in children vary even between countries of similar income levels.

Publicly available data on PCV7 vaccination coverage in European countries is scarce [14-16]. Data on the number of sold PCV7 doses that were actually used, as well as the number of doses used for each child were not available, and PCV7 vaccination coverage could therefore not be calculated in this study. Two different rates were calculated to estimate PCV7 uptake and differences in use between European countries. Firstly, we calculated the number of sold PCV7 doses per 100 live births for the 22 countries for which sales data were available. From the sales data, we also estimated the number of - theoretically possible - complete PCV7 courses per 100 live births for the three most recent years for which data on sales and births were available (Figure 2). We assumed that all PCV7 doses sold in a specific year were given only to children born in that same year, that PCV7 doses were offered according to the vaccination schemes (3+1 or 2+1) recommended in each country at the time, and that the vaccination scheme was completed in the same year. We are aware that this rather simplistic approach is likely to have overestimated the real number of completed vaccination courses. However, it made it easier to benchmark the PCV7 use in the countries.

In Belgium, Denmark and the United Kingdom, the estimates of complete PCV7 courses, based on the respective PCV7 vaccination schemes in use, were above 100% just after the start of the vaccination programme. This could be an indication of increased efforts at the beginning of the programme to include every child in the target group definition.

PCV7 sales were high in countries with a national programme for universal childhood vaccination for pneumococcal disease. They were also remarkably high in Portugal and Spain, countries that do not have such a universal programme. Spain has had a risk-based PCV7 vaccination programme since 2001 and a single universal programme in the Madrid region since 2006 [17]. A study performed in northern Portugal in 2002 aimed at estimating the use of meningococcal and pneumococcal vaccine, which were

both not part of the Portuguese childhood vaccination schedule at the time. That study showed that one third of the 1,877 children born in northern Portugal in 1999 were vaccinated against pneumococcal disease and that most of these children had been vaccinated at an age over 23 months, i.e. later than during the age range recommended in most other countries [18]. The application of both vaccines – the one for meningococcal and the one for pneumococcal disease – was highly correlated. The high vaccine use in the absence of a programme or reimbursement policies was attributed by the authors, at least partly, to high media coverage during a peak of meningitis cases in the region. This single study, however, cannot explain the regular high annual sales of PCV7 in this country.

In conclusion, our study showed large variations in the recommended PCV7 vaccination schemes and in PCV7 use across Europe. While it has to be said that higher vaccine uptake is not always related to the presence of a national vaccination programme, this observation highlights the need for harmonisation of the decision making process in the EU in order to improve access of all European citizens to preventive services such as vaccination. As for other vaccine-preventable diseases, epidemiological surveillance is paramount to provide decision makers with solid data on burden of disease and impact of vaccination. Detailed data on pneumococcal strains circulating in children are currently lacking in many European countries. New conjugated pneumococcal vaccines with broader serotype coverage are under licensure review and more are under development. In this context, establishing surveillance of pneumococcal disease, collection of information on circulating strains and whether these strains are covered by PCV7, as well as surveillance of upcoming conjugated pneumococcal vaccines, is a priority for Europe.

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