

# Recommendations for Pneumococcal Immunization Outside Routine Childhood Immunization Programs in Western Europe

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## ABSTRACT

The global burden of pneumococcal diseases is high, with young children and adults  $\geq 50$  years of age at highest risk of infection. Two types of vaccine are available for the prevention of pneumococcal diseases caused by specific *Streptococcus pneumoniae* serotypes: the pneumococcal polysaccharide vaccine (PPV23) and the pneumococcal conjugate vaccine (PCV7, PCV10, and PCV13). Despite pneumococcal immunization programs in adults and children, the burden in adults has remained high. Most European countries have national or local/regional vaccination recommendations. The objective of this review was to provide an overview of the government recommendations for pneumococcal vaccination outside routine childhood vaccination programs for 16 Western European

countries as of August 2014. We found that recommendations for pneumococcal immunization across Europe are complex and vary greatly among countries in terms of age groups and risk groups recommended for vaccination, as well as which vaccine should be administered. Clarifying or simplifying these recommendations and improving their dissemination could help to increase pneumococcal vaccine uptake and decrease the high burden of pneumococcal diseases in adults, both through a direct effect of the vaccine and via a herd effect in unvaccinated individuals.

**Keywords:** Age; Europe; Immunization; Infectious diseases; Pneumococcal conjugate vaccine; Pneumococcal diseases; Pneumococcal polysaccharide vaccine; Recommendations; Reimbursement; Risk

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## INTRODUCTION

Pneumococcal infection causes a spectrum of diseases from mild presentations such as sinusitis and otitis media, to more serious

diseases such as meningitis, bacteremia, and pneumonia [1]. The 23-valent pneumococcal polysaccharide vaccine (PPV) was introduced in 1983 and is available in Europe for immunization against pneumococcal diseases caused by the 23 serotypes contained in the vaccine (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F) in adults and children aged  $\geq 2$  years [2]. The first pneumococcal conjugate vaccine (PCV7) was licensed in 2000 for immunization against pneumococcal diseases, including sepsis, meningitis, pneumonia, bacteremia, and acute otitis media (AOM) caused by the seven serotypes contained in the vaccine (4, 6B, 9V, 14, 18C, 19F, and 23F) in infants and children aged 2 months to 5 years [3]. PCV10 (serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F) was approved in 2009 for protection against invasive pneumococcal disease (IPD), pneumonia, and AOM in infants and children aged from 6 weeks up to 5 years [4]. A higher-valent PCV, PCV13, comprising six additional serotypes to PCV7 (serotypes 1, 3, 5, 6A, 7F, and 19A) is now available in Europe for the prevention of IPD in adults aged  $\geq 18$  years, and for the prevention of IPD, pneumonia, and AOM in infants and children aged between 6 weeks and 17 years [5].

The global burden of pneumococcal diseases is high, with young children and adults  $\geq 50$  years of age at particular risk of infection. In the 1990s, the age groups with the highest incidence of IPD and highest case fatality rates were infants aged  $< 2$  years and adults aged  $> 50$  years [6]. Routine childhood pneumococcal immunization programs have helped to alleviate the burden of disease in children [7, 8]. Since 2006, the World Health Organization (WHO) has recommended that PCV be included

in all routine childhood immunization programs [9]. Consequently, PCV use has increased from 1% of all WHO member states in 2000 to 44% in 2012, representing 31% of the global birth cohort [9]. Of the European region member states, 49% had introduced PCV by 2012 [9]. Over time the benefits of childhood vaccination with PCV in countries with high uptake have extended to unvaccinated children and adults as a result of the herd effect [10–13]. However, despite pneumococcal immunization programs covering adults and children, the burden in adults has remained high [14].

Recommendations for pneumococcal immunization across Europe are complex and are regularly updated. The objective of this review is to provide an overview of current government recommendations (not including scientific society recommendations), both national and regional where applicable, outside routine pneumococcal immunization programs for infants and children, in 16 individual countries across Western Europe (Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, The Netherlands, Norway, Portugal, Spain, Sweden, and the United Kingdom [UK]), as of August 2014. A summary of the recommendations is provided in the text below, with more detailed information supplied for reference purposes in Table 1. To ensure the most up-to-date information for each country was included, Pfizer's country Medical Affairs offices provided information regarding national and regional recommendations for pneumococcal vaccination. This article is based on pre-existing source material and does not include any studies with human or animal subjects performed by the author.

**Table 1** Comparison of the recommendations and funding for pneumococcal immunization outside routine vaccination programs for children in Western European countries

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
Austria [28]	PCV13/PPV23	National (2014)	At risk and high risk ( $\geq 6$ )	High risk Asplenia (anatomical, functional) Chronic renal insufficiency Cochlear implant Complement and properdin deficiency Hematopoietic organ disorder HIV Hypogammaglobulinemia Immunodeficiency (congenital, acquired) Liquor fistula Nephritic syndrome Nephrotic syndrome prior to immunosuppressive therapy Neurological disorder (in children) Sickle-cell anemia Transplantation (organ, subsequent to stem cell transplantation) At risk Body weight below third percentile (in infants and children) Chronic cardiovascular disease (except hypertension) Chronic respiratory disease Cirrhosis Diabetes Metabolic disease Neoplastic disease N/a	Private	Näive PCV13 followed by PPV23 after $\geq 8$ weeks Pre-vaccinated with PCV After interval of $\geq 8$ weeks 1xPPV23 Pre-vaccinated with PPV23 After interval of $\geq 8$ weeks 1xPCV13 and after another interval of $\geq 8$ weeks 1xPPV23 again (second PPV23 dose recommended $\geq 5$ years after first PPV23 dose) Investigations ongoing into necessity of further vaccinations
	PCV13/PPV23	National (2014)	All ( $\geq 50$ )		Private	Näive PCV13 followed by PPV23 after 1 year Pre-vaccinated with PCV13 After interval of $\geq 1$ year 1xPPV23 Pre-vaccinated with PPV23 After interval of $\geq 2$ years 1xPCV13 Investigations ongoing into necessity of further vaccinations

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information				
Belgium [29, 30]	PCV13/PPV23	National (2013)	High risk ( $\leq 17$ )	Asplenia	Private	PCV13 (schedule depending on age) followed by PPV23 (revaccination every 5 years for asplenia)				
				Chronic disease (heart, lung, renal)						
				Cochlear implant						
				CSF leak						
				Diabetes (non-stable)						
				Immunodeficiency (congenital, immunosuppressant induced)						
				Metabolic disease						
				Autoimmune disease/immune-mediated inflammatory disease						
				Asplenia			Private	High-risk populations PCV13 followed by PPV23 after at least 8 weeks and revaccination with PPV23 every 5 years Adults aged $\geq 50$ years with certain co-morbidities and all $\geq 65$ years Either PPV23 with 1 revaccination after 5 years or PCV13 followed by PPV23 after 8 weeks with 1 revaccination after 5 years (except $>75$ years who do not require revaccination)		
				Cancer (hematological)						
				Cochlear implant						
				HIV						
				Immunodeficiency						
Transplantation (organ)										
Alcoholism										
Chronic disease (heart, kidney, liver, respiratory)										
Smoking										
N/a										
At risk ( $\geq 50$ )	National (2012)	At risk (any age)	Asplenia (functional)	Limited subsidy (to cover vaccination of at-risk groups and some age groups)	For individuals at risk aged $\geq 6$ years vaccination with PCV13 should be followed by 1 dose of PPV23 after $\geq 8$ weeks					
Cochlear implant										
CSF leak										
History of IPD										
HIV										
Lymphoma										
Splenectomy (completed/planned)										
Transplantation (organ)										
Denmark [31]			PCV13			National (2012)	At risk (any age)	Asplenia (functional) Cochlear implant CSF leak History of IPD HIV Lymphoma Splenectomy (completed/planned) Transplantation (organ)	Limited subsidy (to cover vaccination of at-risk groups and some age groups)	For individuals at risk aged $\geq 6$ years vaccination with PCV13 should be followed by 1 dose of PPV23 after $\geq 8$ weeks

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
			At risk (<18)	Chronic lung disease Cyanotic heart disease Heart failure/insufficiency Hypodynamic respiratory insufficiency Immunodeficiency (excluding agammaglobulinemia and SCID) Nephrotic syndrome Palliative surgery for heart disease Chronic disease (heart, kidney, liver, lung) Diabetes N/a	Private	For individuals at risk vaccination with PCV13 should be followed by 1 dose of PPV23 $\geq$ 8 weeks after PCV13 vaccination
Finland [32]	PCV13	National (2013)	All ( $\geq$ 65) High risk ( $\geq$ 5)	Asplenia (anatomical, functional) Cochlear implant HIV Immunodeficiency (congenital, acquired) Liquor fistula Lymphoma Multiple myeloma Nephrotic syndrome Patients treated with systemic corticosteroids or other immunosuppressants	Private (except stem cell transplantation patients)	PCV13 preferred in high-risk individuals (e.g., immunocompromised) and may be followed by PPV23. However, physicians can choose whether to give PCV13 or PPV23 PCV13 is funded for stem cell transplantation patients of all ages PCV13 may also be considered in healthy individuals of all ages
	PPV23		At risk or in permanent institutional care ( $\geq$ 5)	T transplantation (organ and tissue) Chronic disease (cardiac, pulmonary) Diabetes (type 1) Hepatic insufficiency Patients treated with systemic corticosteroids or other immunosuppressants Renal insufficiency T transplantation (organ, tissue) N/a	-	-
			All ( $\geq$ 65)			

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
France [33]	PCV13	National (2013)	At risk ( $\geq 2$ )	Asplenia or hyposplenia Cancer treated by chemotherapy (solid tumor, hematological) Cochlear implant or planned cochlear implant HIV Immunodeficiency (congenital) Immunosuppressive therapy, biotherapy, or corticotherapy for autoimmune disease or chronic inflammation Meningeal fistula Nephrotic syndrome Transplantation or waiting for transplantation (organ, hematopoietic stem cell)	Public	For all at-risk individuals aged $\geq 2$ years, PCV13 followed by PPV23 after $\geq 8$ weeks In some cases the vaccination schedule may differ and there are slight differences for specific populations (for asplenic and immunosuppressed patients PCV is preferred), but PCV13 should be administered first in all cases For high-risk individuals aged $\geq 6$ years to $< 50$ years funding procedure ongoing
	PPV23		At risk ( $\geq 5$ )	Asthma (severe with continuous treatment) Chronic liver disease (alcoholic or non-alcoholic origin) Chronic respiratory failure COPD Cyanotic congenital heart disease Diabetes (not balanced by diet) Emphysema Heart failure Kidney failure	Public	-

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
Germany [34]	PCV	Saxony [35] (updated January 2014)	At risk (>2)	<p>Asplenia</p> <p>Autoimmune disease</p> <p>Bone marrow transplantation</p> <p>Chronic disease (heart, kidney, respiratory)</p> <p>CSF leaks, cochlea implant</p> <p>HIV</p> <p>Hematological diseases</p> <p>Immunodeficiency (primary)</p> <p>Metabolic disease</p> <p>Neurological diseases in children</p> <p>Occupational risk (laboratory personnel at risk of infection, medical personnel in contact with patients)</p> <p>Sickle-cell anemia</p> <p>T transplantation (organ)</p> <p>N/a</p>	Public	<p>All infants from the age of 2 months to 5 years should receive PCV (vaccination should be started in the third month of life, according to schedule of vaccine manufacturer)</p> <p>PCV may be PCV10 or PCV13 for those aged 2–&lt;5 years; PCV will be PCV13 for those aged ≥5 years. Children with persisting risk for pneumococcal infection should be vaccinated in the third year of life with PPV23 in addition to PCV (interval of at least 2 months after last vaccination with PCV)</p> <p>Non-vaccinated infants (aged ≥5 years), adolescents and adults should receive one dose of PCV or PPV23 (according to approval)</p> <p>PCV can be supplemented with PPV23 if protection against further serotypes is required (interval at least 4 years)</p> <p>In those pre-vaccinated with PPV23, catch-up vaccination with PCV is useful (interval at least 5 years)</p> <p>In at-risk individuals and those aged ≥60 years revaccination with PPV23 is possible (≥5 years for adults, ≥3 years for children aged &lt;10 years)</p> <p>For this age group, PCV may be PCV10 or PCV13</p> <p>For congenital or acquired immunodeficiencies, chronic renal diseases/nephrotic syndrome, revaccination can be considered every 5 years (for those aged &gt;10 years) or every 3 years (for those aged &lt;10 years)</p>
	PCV	National (PCV funding 2013; PCV recommendations 2014)	At risk (2–<5)	<p>Chronic disease (e.g. heart, kidney, liver, respiratory diseases, metabolic disorders [e.g. diabetes], neurological diseases [e.g. cerebral paretoses, seizure disorders])</p> <p>Immunodeficiency (congenital, acquired, e.g. T cell, B cell or antibody deficiency, deficiency or functional disorders of myeloid cells [e.g. neutropenia, chronic granulomatosis leukocyte adhesion or signal transduction defects], complement or properdin deficiency, functional hypersplenism or splenectomy, neoplastic diseases, HIV infection, bone marrow transplantation, immunosuppressive therapy [e.g. due to organ transplantation, autoimmune disease])</p> <p>Anatomic risks, risks associated with foreign bodies for pneumococcal meningitis (e.g. liquor fistula, cochlea implant)</p>		

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
	PCV13/PPV23	National (PCV funding 2013; PCV recommendations 2014; PPV 1982)	At risk ( $\geq 5$ )	Chronic disease (e.g., heart, kidney, liver, respiratory diseases, metabolic disorders [e.g., diabetes], neurological diseases [e.g., cerebral palsy, seizure disorders]) Immunodeficiency (congenital, acquired, e.g., T cell, B cell or antibody deficiency, deficiency or functional disorders of myeloid cells [e.g., neutropenia, chronic granulomatosis, leukocyte adhesion or signal transduction defects], complement or properdin deficiency, functional hypersplenism or splenectomy, neoplastic diseases, HIV infection, bone marrow transplantation, immunosuppressive therapy [e.g., due to organ transplantation, autoimmune disease]) Anatomic risks, risks associated with foreign bodies (e.g., liquor fistula, cochlea implant)		For this age group, PCV will be PCV13 For congenital or acquired immunodeficiencies, chronic renal diseases/nephrotic syndrome, revaccination can be considered every 5 years (for those aged $>10$ years) or every 3 years (for those aged $<10$ years)
Greece [36]	PPV23 PCV13	National (1998) National (2011)	All ( $\geq 60$ ) All ( $>50$ )	N/a N/a	Public	-
Ireland [37]	PCV13/PPV23	National (2013)	Medium risk and high risk ( $2- <5$ )	Medium risk Children $<5$ years of age following IPD Chronic heart, lung, or liver disease Chronic renal disease or nephrotic syndrome Diabetes mellitus requiring insulin or oral hypoglycemic drugs Down syndrome High risk Asplenia, hyposplenism (including splenectomy, sickle-cell disease, hemoglobinopathies, and celiac disease) Candidates for, or recipients of, a cochlear implant Complement deficiency (particularly C1-C4) CSF leaks (congenital or complicating skull fracture or neurosurgery) Immunosuppressive conditions (e.g., some B and T cell disorders, HIV infection, leukemia, lymphoma) and those receiving immunosuppressive therapies Intracranial shunt Post-hematopoietic stem cell transplant Solid organ transplant	Public PCV13 supplied free of charge to all those in risk groups; individuals pay an administration fee	2-5 years: 1 or 2 doses of PCV13 at 2-month intervals followed by 1 dose of PPV23 $\geq 2$ months after final PCV dose



Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
			High risk (5–<18; 18–64)	Asplenia, hyposplenia (including splenectomy, sickle-cell disease, hemoglobinopathies, and celiac disease) Candidates for, or recipients of, a cochlear implant Complement deficiency (particularly C1–C4) CSF leaks (congenital or complicating skull fracture or neurosurgery) Immunosuppressive conditions (e.g., some B and T cell disorders, HIV infection, leukemia, lymphoma) and those receiving immunosuppressive therapies Intracranial shunt Post-hematopoietic stem cell transplant Solid organ transplant	PCV13 supplied free of charge to all those aged <18 years in risk groups; individuals pay an administration fee PCV13 is not free of charge to those aged ≥18 years PPV23 supplied free of charge to all those in risk groups; individuals pay an administration fee unless they have a medical or doctor-only card	>5–<18 years: 0, 1 or 2 doses of PCV13 followed by 1 dose of PPV23 ≥2 months after PCV
	PPV23		Medium risk (5–<18)	Children <5 years of age following IPD Chronic heart, lung, or liver disease Chronic renal disease or nephrotic syndrome Diabetes mellitus requiring insulin or oral hypoglycemic drugs Down syndrome	Vaccine supplied free of charge to all those in risk groups; individuals pay an administration fee unless they have a medical or doctor-only card	1 Dose of PPV23
			Medium risk (18–64)	Chronic heart, lung, or liver disease Chronic renal disease or nephrotic syndrome Diabetes mellitus requiring insulin or oral hypoglycemic drugs Smokers and alcoholics Individuals with occupational exposure to metal fumes (i.e., welders)		–
			All (≥65)	N/a		

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
Italy	PCV13/PPV23	Basilicata [38] (2012)	At risk (any age)	Chronic disease (heart, liver [hepatic cirrhosis], respiratory)	Public	For at-risk adults aged <50 years, PCV13 is recommended in addition to PPV23, PPV23 should be administered after >8 weeks
		Bolzano [39] (2013)	All ( $\geq 65$ ) At risk (any age)	Metabolic disease N/a Alcoholism Asplenia Chronic disease (cardiac, liver, pulmonary) Cirrhosis Cochlear implant Diabetes HIV Immunodeficiency Immunosuppression (clinically significant) Leukemia Liquor fistula Lymphoma Multiple myeloma Neoplastic spread Nephrotic syndrome SCID Thalassemia Transplantation (organ, bone marrow)	Public	-
		Cagliari (LHU Cagliari 8) [40] (2011)	All ( $>65$ ) At risk ( $\geq 50$ )	N/a Asplenia Chronic disease (heart, kidney, liver, respiratory) Cochlear implant CSF leak HIV Immunodeficiency Metabolic disease Other pathologies predisposed to high IPD risk Transplantation (organ)	Public	PCV13 recommended in addition to PPV23 PPV23 to be administered 8 weeks following PCV13

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
Emilia Romagna [41]		(2014)	At risk and high risk (any age)	High risk Asplenia Chronic disease (kidney [renal failure]) Cochlear implant CSF leak Hemoglobinopathy HIV Immunodeficiency (acquired) Immunosuppression (iatrogenic) Leukemia Lymphoma Multiple myeloma Neoplastic spread Nephrotic syndrome Transplantation (organ, bone marrow) At risk Alcoholism Chronic disease (heart, liver [hepatic cirrhosis], respiratory) Diabetes Residents in an institution (e.g. nursing home) aged >65 years N/a	Public	High-risk individuals PPV23 recommended in addition to PPV23 PPV23 should be administered $\geq 8$ weeks after PCV13; for bone marrow transplantation, 3 doses of PCV13 (interval 2 months); a fourth dose is recommended in case of chronic graft versus host disease
Friuli-Venezia Giulia [42]		(2012)	In permanent institutional care ( $\geq 65$ ) At risk ( $\geq 18$ )	Asplenia Chronic disease (heart, kidney [renal failure], liver [hepatic cirrhosis], respiratory) CNS disease Metabolic disease Others N/a	Public	PPV23 recommended in addition to PPV23 At-risk individuals: PCV13, 2 doses, 8 weeks apart (3 doses for bone marrow transplantation)
			All ( $\geq 65$ )			

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
		Lazio [43] (2012)	At risk (any age)	Asplenia Chronic disease (heart, kidney [renal failure], liver [hepatic cirrhosis], respiratory) CNS disease Metabolic disease	Public	-
		Liguria [44] (2013)	At risk (any age)	Asplenia Cancer (hematological) Chronic disease (heart, kidney [renal failure], liver [hepatic cirrhosis], respiratory) CSF leak Diabetes Immunodeficiency (congenital, acquired) Neoplastic spread Transplantation (organ, bone marrow)	Public	-
		Lombardia (LHU Milan) [45] (2012)	All (>70) At risk and high risk (>18)	N/a High risk Asplenia Chronic disease (renal) Cochlear implant CSF leak Hemoglobinopathy HIV Immunodeficiency (congenital, acquired) Leukemia Lymphoma Multiple myeloma Neoplastic spread Previous IPD Transplantation (organ, bone marrow) At risk Chronic disease (heart, liver, pulmonary) Diabetes	Public (PCV13 is available on medical prescription)	PCV13 recommended in addition to PPV23 PPV23 should be administered 8 weeks after PCV13 Individuals already vaccinated with PPV23 should be vaccinated with PCV13 1 year after PPV23 For adults aged <50 years PPV23 is recommended For adults aged ≥50 years PCV13 is recommended

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
			All ( $\geq 65$ )	N/a		PCV13 if not previously vaccinated
		Marche [46] (2013)	At risk (any age)	Asplenia	Public	-
				Chronic disease (heart, kidney disease [renal failure], respiratory)		
				Cochlear implant		
				CSF leak		
				Diabetes		
				Hepatic cirrhosis and chronic liver disease due to alcoholism		
				HIV		
				Immunodeficiency (congenital, acquired)		
				Immunosuppression (iatrogenic)		
				Leukemia		
				Lymphoma		
				Multiple myeloma		
				Neoplasia		
				Thalassemia		
				Transplantation (organ, bone marrow)		
		Piemonte [47] (2012)	At risk ( $>5$ )	Asplenia	Private	PCV13 + PPV23 6 months apart
				Chronic disease (heart [excluding hypertension], kidney [renal failure], liver, respiratory)		
				Cochlear implant		
				Complement deficiency		
				CSF leak		
				Diabetes (type 1)		
				Hemoglobinopathy		
				Immunodeficiency (congenital, acquired)		

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
		Puglia [48] (2012)	At risk ( $\geq 50$ )	Asplenia Chronic disease (heart, kidney [renal failure], liver [hepatic cirrhosis], respiratory) Cochlear implant CSF leak Diabetes Hemoglobinopathy HIV Immunodeficiency (congenital, acquired) Leukemia Lymphoma Multiple myeloma Neoplasia N/a	Public	-
		Sicilia [49] (2012)	Cohort (65, 70, 75) At risk (50–64)	Asplenia Chronic disease (heart, kidney [renal failure], liver [hepatic cirrhosis], respiratory) CNS disease Metabolic disease N/a	Public	-
		Trento [50] (2012)	Cohort (65, 75) At risk or nursing home residents (any age)	Asplenia Chronic cardiac disease Chronic renal failure Cochlear implant COPD Diabetes HIV Immunodeficiency (congenital) Immunosuppression Liquor leakage Nephrotic syndrome SCID	Public	-

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
		Tuscany LHU [51] (Local Directive to GPs—April 2012) (2012)	At risk or in permanent institutional care ( $\geq 6$ )	All ( $>65$ ) Asplenia Cardiac decompensation (severe) Chronic disease (hematopoietic, liver) Chronic renal failure COPD Diabetes Immunodeficiency	N/a Public	-
		Umbria [52] (2012)	All ( $\geq 50$ ) At risk or in permanent institutional care ( $\geq 50$ )	N/a Asplenia Chronic disease (heart, kidney [renal failure], liver [hepatic cirrhosis], respiratory) CNS disease Metabolic disease	Public	-
		Veneto [53] (2012)	At risk (any age)	Asplenia Cancer (hematological, solid) Chronic disease (heart, kidney [renal failure], liver [hepatic cirrhosis], respiratory) CNS disease Immunodeficiency (primary) Metabolic disease Transplantation (organ)	Public	-

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
	PPV23	National [54] (2005)	At risk (any age)	Agammaglobulinemia Asplenia Asthma Autoimmune disease Cancer (hematological, solid tumor) Chronic disease (heart, kidney, liver, respiratory) Cyanotic heart disease Immunodeficiency (primary) Metabolic disease SCID	Public	-
Luxembourg [55, 56]	PCV13	National (2011)	At risk (<5)	Transplantation (organ) Asplenia Chronic disease (heart, liver, renal, respiratory [excluding asthma]) Cochlear implant CSF leak Diabetes HIV Immunocompromised Premature birth	Private	-



Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
	PPV23	National (2008)	At risk or in permanent institutional care ( $\geq 18$ )	Alcoholism Asplenia Chronic disease (cardiovascular, renal, respiratory) Cirrhosis Cochlear implant CSF leak Diabetes HIV Liquor fistula Lymphoma Multiple myeloma Nephrotic syndrome Sickle-cell disease T transplantation (organ)		-
Netherlands [57]	PCV13/PPV23	National (2012)	All (>60) At risk (any age)	N/a Asplenia	Private	1 Dose of PCV13 followed by 1 dose of PPV23 after $\geq 8$ weeks PPV23 should be repeated once after 5 years
Norway [58, 59]	PCV13	National (2013)	At risk (any age)	Asplenia HIV Stem cell transplantation Considered for following groups after collective evaluation of risk: B cell deficiency Cancer (hematological) Cochlear implant CSF leak T transplantation (organ, bone marrow)	Public (for asplenia, HIV, and stem cell transplantation only)	PCV13 recommended only in addition to PPV23 Administer PCV13 $\geq 8$ weeks prior to PPV23 For asplenia and HIV administer PPV23 in addition to PCV13 Repeat PPV23 every 5 years for asplenia and every 10 years for other risk groups

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
	PPV23		At risk (any age)	Asplenia B cell deficiency Cancer (hematological) Cochlear implant CSF leak HIV Transplantation (organ, bone marrow)		
Portugal [60]	PCV13	National (2010)	All ( $\geq 65$ ) At risk and high risk ( $< 59$ months)	N/a High risk Asplenia (anatomical, functional) Cochlear implant or cochlear implant placement planned Down syndrome HIV infection Premature birth ( $\leq 28$ weeks) Sickle-cell disease and other hemoglobinopathies Presumable high risk Acquired immunodeficiency Immunosuppressive therapy, prolonged corticosteroid therapy, chemotherapy, or radiotherapy Hematological cancer, mainly lymphocytic leukemia (acute and chronic), Hodgkin disease and multiple myeloma Bone marrow donor Chronic disease (cardiac [cyanotic congenital cardiopathy, heart failure], liver, pulmonary [excluding asthma, except patients on high doses of corticosteroids]) Chronic renal failure Congenital immunodeficiency Diabetes CSF fistula (congenital malformation, cranial fracture, or neurosurgery procedure) Nephrotic syndrome Organ or bone marrow transplantation	Public	-

**Table 1** continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
	PPV23		At risk and high risk (2–17)	<p>High risk</p> <p>Asplenia (anatomical, functional)</p> <p>Cochlear implant or cochlear implant placement planned</p> <p>Down syndrome</p> <p>HIV infection</p> <p>Premature birth (<math>\leq 28</math> weeks)</p> <p>Sickle-cell disease and other hemoglobinopathies</p> <p>Presumable high risk</p> <p>Acquired immunodeficiency</p> <p>Immunosuppressive therapy, prolonged corticosteroid therapy, chemotherapy, or radiotherapy</p> <p>Hematological cancer, mainly lymphocytic leukemia (acute and chronic), Hodgkin disease and multiple myeloma</p> <p>Bone marrow donor</p> <p>Chronic disease (cardiac [cyanotic congenital cardiopathy, heart failure], liver, pulmonary [excluding asthma, except patients on high doses of corticosteroids])</p> <p>Chronic renal failure</p> <p>Congenital immunodeficiency</p> <p>Diabetes</p> <p>CSF fistula (congenital malformation, cranial fracture, or neurosurgery procedure)</p> <p>Nephrotic syndrome</p> <p>Organ or bone marrow transplantation</p> <p>Cancer (hematological)</p> <p>Chemotherapy or immunosuppressive treatment</p> <p>HIV</p> <p>Nephrotic syndrome</p> <p>Renal insufficiency</p> <p>Transplantation (organ, hematopoietic cell)</p>		
Spain [61]	PCV13	National (2012)	At risk ( $\geq 50$ )		Public	-

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
		Cataluña [62] (2014)	At risk ( $\geq 5$ )	Asplenia or asplenic dysfunction Cancer (hematological) Cochlear implant CSF leak HIV Immunodeficiency (congenital, acquired) Immunosuppressive treatment, including systemic steroids and radiotherapy Nephrotic syndrome Renal insufficiency Sickle-cell disease Transplantation		
		Galicia [63] (2012)	At risk ( $\geq 50$ )	Asplenia Cancer (hematological) Chemotherapy or immunosuppressive treatment Chronic renal disease (stage $\geq 3$ ) Cochlear implant CSF leak HIV Nephrotic syndrome Transplantation (organ, hematopoietic cell)		
		Murcia [64] (2014)	At risk ( $\geq 6$ )	Asplenia or asplenic dysfunction B or T cell deficiency Cancer (hematological) Chemotherapy or radiotherapy Chronic liver disease (including cirrhosis) Chronic renal insufficiency (advanced) Complement deficiency Hemodialysis History of IPD HIV Phagocytosis dysfunction Transplantation (organ, hematopoietic cell)		

**Table 1** continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
			At risk (6–50)	Cochlear implant		
				CSF leak		
		Basque Country [65] (2013)	At risk ( $\geq 50$ )	Asplenia		
				Cancer (hematological)		
				Chemotherapy or immunosuppressive treatment		
				Chronic renal insufficiency (advanced)		
				Cochlear implant		
				CSF leak		
				Hemodialysis		
				History of IPD		
				HIV		
				Immunodeficiency (congenital, acquired)		
				Transplantation (organ, hematopoietic cell)		
		Valencia [66] (2013)	At risk ( $\geq 18$ )	Asplenia or splenic dysfunction		
				B or T cell deficiency		
				Cancer (hematological)		
				Chemotherapy or radiotherapy		
				Chronic renal disease (stage $\geq 3$ )		
				Complement deficiency		
				Cochlear implant		
				CSF leak		
				Hemodialysis		
				HIV		
				Nephrotic syndrome		
				Phagocytosis dysfunction		
				Transplantation (organ, hematopoietic cell)		

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
		Madrid [67] (2013)	At risk (≥50)	Asplenia (including elective splenectomy and late complement component deficiency) Cancer (hematological) Chemotherapy or immunosuppressive treatment Chronic alcoholism Chronic liver disease Cirrhosis Coagulation factor concentrate recipients Cochlear implant CSF leak Hemodialysis HIV Nephrotic syndrome Renal disease (end-stage) Renal insufficiency Sickle-cell disease		
		Navarra [68] (2013)	At risk (≥18)	Transplantation (organ, hematopoietic cell) Asplenia Cancer (hematological) Chemotherapy or immunosuppressive treatment HIV Nephrotic syndrome Renal insufficiency (severe) Transplantation (organ, hematopoietic cell)		
		Extremadura [69] (2013)	At risk (≥50)	Cancer (hematological) Chemotherapy or immunosuppressive treatment HIV Nephrotic syndrome Renal insufficiency Transplantation (organ, hematopoietic cell)		

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
	PPV23	All Spanish autonomous regions [70] (varies)	At risk or older adults in permanent institutional care ( $\geq 2$ to $\leq 60/65$ )	Alcoholism Asplenia Cancer (hematological) Chronic disease (cardiovascular, respiratory) Cirrhosis Cochlear implant Diabetes HIV Nephrotic syndrome Renal insufficiency Sickle-cell disease Transplantation (organ) N/a		Funded by Public Health of the different Spanish Regions Date of implementation differs between the 19 different autonomous regions
		Most Spanish autonomous regions [70] (varies)	All ( $\geq 60/\geq 65$ )			Recommended vaccination by age at time of influenza vaccination campaign Date of implementation varies between different regions
Sweden	PCV13/PPV23	Stockholm [71] (2013)	At risk ( $\geq 2$ )	Asplenia Cochlear implant Cystic fibrosis Immunosuppression (e.g. transplantation, receiving cytostatics or other medication severely affecting the immune system) Liquor fistula Nephrotic syndrome Transplantation (organ)	Public (for high-risk individuals)	Regional recommendations for high-risk individuals in Stockholm, PCV13 recommended followed by PPV23 after $\geq 8$ weeks

Table 1 continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
	PPV23	National [72] (1994)	At risk ( $\geq 2$ )	Agammaglobulinemia Alcoholism Asplenia Asthma Autoimmune disease Cancer (hematological, solid tumor) Chronic disease (heart, kidney, liver, respiratory) Cyanotic heart disease CNS disease CSF leak Hemodynamically significant residual lesion after surgery Hemodynamic respiratory insufficiency History of IPD HIV Immunodeficiency (primary) Intracranial shunt Metabolic disease SCID Sickle-cell disease and other hemoglobinopathies Transplantation (organ)	Varies	Funding is decided by the local county council, in some areas vaccination of individuals aged $\geq 65$ years is free of charge, in other areas it is partially subsidized, and in the remainder the full cost is paid by the individual
United Kingdom	PCV13 [73]	National (2013)	All ( $\geq 65$ ) At risk ( $< 5$ )	Asplenia Asthma (only if high-dose systemic steroids) Cancer (hematological, solid tumor) Chronic disease (heart, kidney, liver, respiratory) Cochlear implant CSF leak Diabetes (excludes diet controlled) HIV Immunosuppression Sickle-cell disease Transplantation (organ)	Via the National Health Service	-



**Table 1** continued

Country	Recommended vaccine	Region (date of recommendations)	Population (age, years)	Definition of risk	Funding	Additional information
			At risk—severely immunocompromised (≥5)	Genetic disorders severely affecting the immune system (e.g., IRAK-4, NEMO, complement deficiency) Leukemia (acute, chronic) Multiple myeloma Transplantation (bone marrow) Asplenia		
	PPV23 [73]	National (1992)	At risk (≥2)	Asthma (only if high-dose systemic steroids) Cancer (hematological, solid tumor) Chronic disease (heart, kidney, liver, respiratory) Cochlear implant CSF leak Diabetes (excludes diet controlled) HIV Immunosuppression Sickle-cell disease Transplantation (organ) N/a		
		National (2003)	All (≥65)			

*CMS* Central nervous system, *COPD* chronic obstructive pulmonary disease, *CSF* cerebrospinal fluid, *GP*s general practitioners, *HIV*/human immunodeficiency virus, *IPD* invasive pneumococcal disease, *LHU* local health unit, *N/a* not applicable, *PCV* pneumococcal conjugate vaccine, *PPV* pneumococcal polysaccharide vaccine, *SCID* severe combined immunodeficiency

## RECOMMENDATIONS OUTSIDE ROUTINE IMMUNIZATION PROGRAMS FOR CHILDREN FOR PNEUMOCOCCAL IMMUNIZATION IN WESTERN EUROPE

In addition to routine pneumococcal immunization programs in infants and children, most countries across Europe have further local or national recommendations (Table 1). Those without such recommendations may follow other guidelines, such as society guidelines or those from the Advisory Committee on Immunization Practices (ACIP; e.g., The Netherlands). Although generally falling within the prescribing information for the vaccines, pneumococcal immunization practices differ across Europe with regards to age groups and risk groups immunized, which vaccine (PPV versus PCV) is advised for which groups, and eligibility for reimbursement. The majority of the 16 Western European countries included in this article implement immunization programs with both age-based and risk-based elements. PPV23 is widely recommended across Western Europe; however, many countries have now included PCV in their pneumococcal immunization recommendations for certain groups of children and adults, either alone or in addition to PPV23. Figure 1 details the current adult national recommendations and reimbursement of PCV13.

### Age-Based Elements of Pneumococcal Immunization Programs

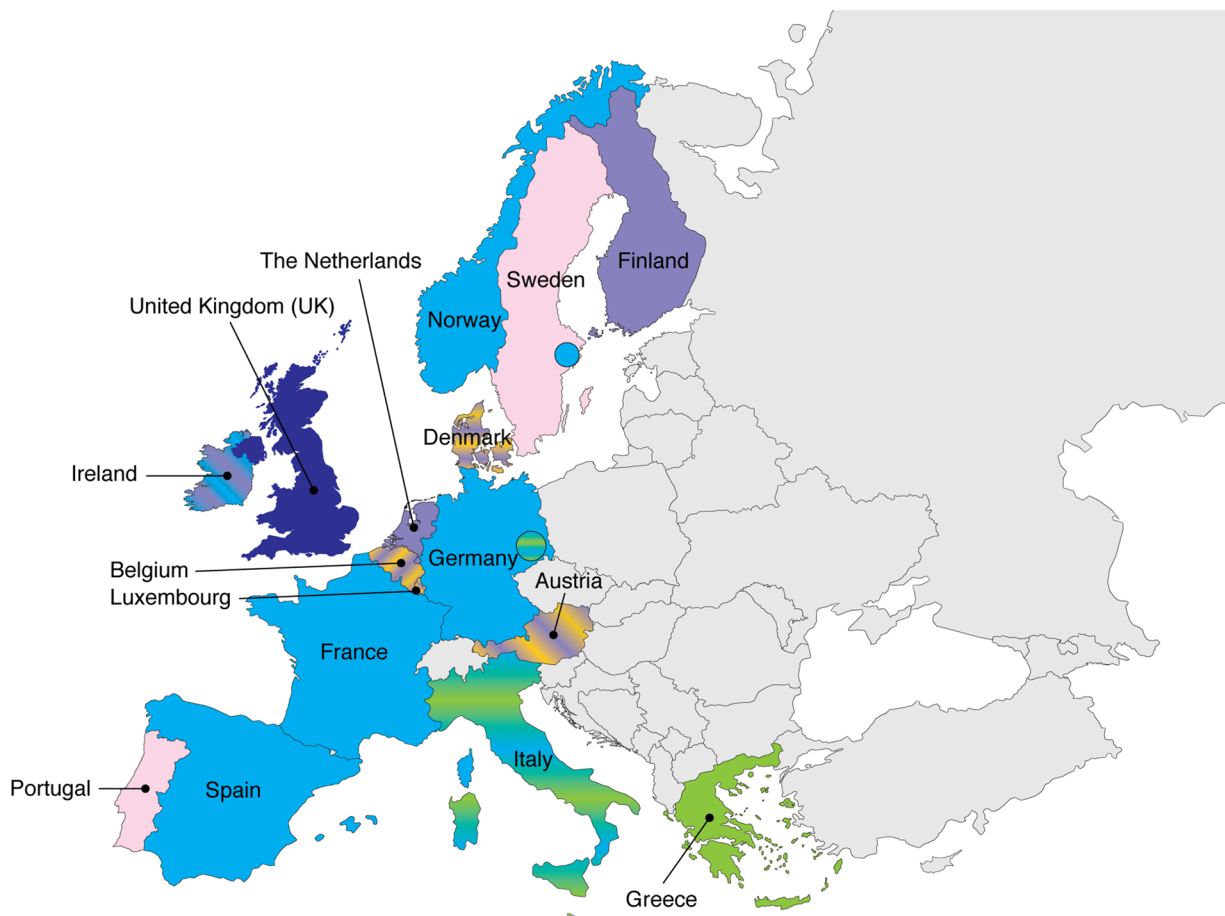
Age-based recommendations (usually for older adults) form part of the full immunization programs across most countries in Western

Europe. However, the recommended vaccine and the age group eligible for vaccination vary between countries (Table 1). For example, immunization programs recommending PPV23 are implemented in Luxembourg (age >60 years), Finland, Ireland, Norway, Sweden, UK (all age  $\geq 65$  years), and most autonomous regions of Spain (age  $\geq 60/\geq 65$  years). Immunization programs recommending PCV exist in Greece (PCV13; >50 years), Germany (Saxony only; PCV;  $\geq 60$  years), Denmark (PCV13;  $\geq 65$  years), and some regions of Italy, including Tuscany (PCV13;  $\geq 50$  years), Basilicata, Bolzano, and Trento (all PCV13; >65 or  $\geq 65$  years), Liguria (PCV13; >70 years), Puglia (PCV13; cohorts 65, 70, 75 years), and Sicilia (PCV13; cohorts 65, 75 years). Additionally, age-based immunization programs recommending PCV and/or PPV23 exist in Austria, Belgium, and some regions of Italy.

### Risk-Based Elements of Pneumococcal Immunization Programs

Some countries/regions across Western Europe advise pneumococcal immunization in individuals with specific co-morbidities that are considered to place them at an increased risk of pneumococcal diseases, regardless of age. Such purely risk-based elements are implemented in the pneumococcal immunization programs in Denmark, Norway, Sweden, UK, and some regions of Italy (Basilicata, Bolzano, Emilia Romagna, Lazio, Liguria, Marche, Trento, and Veneto; see Table 1 for specific risk groups and recommended vaccines).

Risk-based elements of pneumococcal immunizations programs across Europe can be very complex. For example, the risk groups eligible for vaccination can vary by age group (e.g., Belgium, Denmark, France, Germany,



**Fig. 1** European national recommendations and reimbursement of 13-valent pneumococcal conjugate vaccine (PCV13) in adults

Ireland, Luxembourg, Spain [Murcia], and the UK), different vaccines may be advised for different risk groups (e.g., Finland, France, Ireland, Norway, and the UK) or different vaccines may be advised in different age groups considered to be at risk of pneumococcal diseases (e.g., France, Germany, Ireland, Luxembourg, and Portugal). Many

European countries/regions advise vaccination with both PCV and PPV23 in individuals at risk of pneumococcal diseases (see the Additional information column in Table 1). However, PCV is preferred over PPV23 in individuals at risk of pneumococcal diseases in Finland (all high-risk individuals) and France (immunosuppressed and asplenic individuals).

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## Heterogeneity in the Definition of Individuals Considered to be at Risk of Pneumococcal Diseases

There is a marked variation between countries concerning which individuals are considered to be at risk of pneumococcal diseases and their eligibility for immunization, with some countries including many more medical conditions (e.g., Austria, Ireland, and Portugal) than others (e.g., Norway and national recommendations for Spain). Consistent with the ACIP recommendations for immunization of children and adults at risk of pneumococcal diseases [15, 16], common conditions considered to place individuals at an increased risk in Europe include underlying comorbidities such as chronic kidney (risk category in adults only), heart, liver or respiratory disease, metabolic diseases (e.g., diabetes mellitus), central nervous system diseases (e.g., cerebrospinal fluid leak) and immunocompromised individuals, including human immunodeficiency virus (HIV)-positive individuals, primary immunodeficiency, organ transplantation, asplenia (functional or anatomical), and hematological cancer. Other risk factors less commonly included are previous IPD (Denmark, Ireland [children under the age of 5 years], Italy [Lombardia], Spain [Murcia and Basque Country], and Sweden) and lifestyle risk factors such as alcoholism (Belgium, Ireland, Italy [Bolzano and Emilia Romagna], Luxembourg, Spain [Madrid and all autonomous regions], and Sweden), smoking (Belgium and Ireland), and residing in a nursing home or permanent institution (Finland, Italy [Emilia Romagna, Trento, Tuscany, Umbria], Luxembourg, and Spain [all autonomous regions]). Most European countries recommend initial vaccination with PCV13 for individuals at risk of pneumococcal

diseases, followed by PPV23 vaccination  $\geq 8$  weeks later. Although broadly in line with ACIP recommendations [15, 16], age groups and timing of vaccination vary between countries.

## Funding of Pneumococcal Immunization Programs

Further differences between countries across Europe also relate to public reimbursement for pneumococcal immunization. It is not funded for any age or risk groups in Austria, Belgium, or Luxembourg. Partial funding is available in Denmark, Finland (stem cell transplantation patients), Ireland (all individuals receiving PCV <18 years of age and some patients receiving PPV23 at risk of pneumococcal disease required to pay an administration fee; no funding for those aged  $\geq 18$  years), Norway (asplenia, HIV and stem cell transplantation), and Sweden (PCV13 funded in Stockholm county in individuals at high risk of pneumococcal diseases; PPV23 varies regionally between local councils). In contrast, full public funding is provided in France, Germany, Greece, Portugal, Spain, and Italy (except Piemonte).

## Impact of Recommendations and Pneumococcal Immunization on Disease

The impact of pneumococcal immunization is highly dependent on vaccine uptake. Differences in pneumococcal immunization recommendations can impact the rates of immunization between countries. Risk-based immunization programs require the identification of individuals with specific diseases, while targeting of vaccination is simpler for age-based programs and thus they are easier to implement. Countries with age-based recommendations and public

reimbursement have demonstrated a higher uptake of PPV23 than countries immunizing only individuals at risk of pneumococcal diseases or countries without public reimbursement [17].

A meta-analysis of the efficacy of PPV in clinical trials demonstrated a high degree of heterogeneity between trials with little evidence of protection among elderly individuals or adults with chronic respiratory illness, for whom the vaccine was recommended [18]. Similarly, a meta-analysis of randomized controlled trials published up to June 2012 demonstrated the effectiveness of PPV in preventing IPD, but not all-cause pneumonia or mortality in the elderly [19]. However, data are conflicting. For example, in Japanese nursing home residents, PPV23 was shown to reduce the prevalence of pneumococcal pneumonia and all-cause pneumonia, as well as decrease mortality from pneumococcal pneumonia [20]. Although it is too early to assess the long-term impact of the inclusion of PCV in adult immunization programs, estimations can be made based on impact data from PCV7 childhood immunization programs, which have substantially reduced the burden of pneumococcal diseases in children [7, 8]. Emerging impact data in children show a decline in IPD due to serotypes contained in PCV13, following the introduction of PCV13 in Spain, England, and Norway [21–23]. Furthermore, it is anticipated that PCV13 will be cost-effective. Cost-effectiveness studies have predicted net savings of 102 million Euros over 5 years based on a model of a 65-year-old cohort immunization campaign in Spain [24], and between 7 million and 19 million Euros based on a model of an age-based PCV13 immunization program in adults aged  $\geq 65$  years in Italy [25].

## CONCLUSION

Young children and adults aged  $\geq 50$  years are at particular risk of pneumococcal infection and despite childhood and adult immunization programs, burden of disease in adults remains high. Since the approval of PCV13 in adults aged  $\geq 50$  years in 2011, PCV13 is gradually being included in recommendations for adult pneumococcal immunization in addition to inclusion in childhood immunization programs within Western European countries. Ultimately, this should help to increase vaccine uptake and decrease the high burden of pneumococcal diseases in adults both through a direct effect of the vaccine and via a herd effect in unvaccinated individuals. Vaccine uptake and the effectiveness of pneumococcal immunization programs could be somewhat increased by raising awareness among healthcare professionals of the burden of pneumococcal diseases in adults, and improving the dissemination of recommendations for pneumococcal immunization. Moreover, the recommendations for pneumococcal immunization can be very complex and vary greatly between European countries in terms of age, risk, and which vaccine should be administered. When revising recommendations, public health officials should consider clarifying or simplifying recommendations, taking into account the merits of age-based versus risk-based recommendation for ease of implementation. This could help to increase vaccine uptake and thus reduce the burden of disease. Furthermore, the Community Acquired Pneumonia Immunization Trial in Adults (CAPiTA; ClinicalTrials.gov #NCT00744263), a randomized placebo-control trial involving  $>84,000$  pneumococcal vaccination-naïve, community-dwelling adults  $\geq 65$  years of age, will provide valid data on the role of adult PCV13 vaccination in preventing vaccine-type

pneumococcal diseases, including pneumococcal community-acquired pneumonia and IPD, and thus has the potential to impact future pneumococcal vaccination recommendations [26, 27].

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**Compliance with ethical guidelines.** This article is based on pre-existing source material and does not include any studies with human or animal subjects performed by the author.

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## REFERENCES

1. World Health Organization. Pneumococcal vaccines WHO position paper—2012. *Wkly Epidemiol Rec.* 2012;87:129–44.
2. Sanofi Pasteur MSD. Pneumovax II solution for injection in a vial: summary of product characteristics. 2013. <http://www.medicines.org.uk/emc/medicine/1446/SPC/Pneumovax+II/>. Accessed Sept 29, 2014.
3. Pfizer. Prevenar: summary of product characteristics. 2013. [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-\\_Product\\_Information/human/000323/WC500041563.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000323/WC500041563.pdf). Accessed Sept 29, 2014.
4. GlaxoSmithKline. Synflorix suspension for injection in pre-filled syringe: summary of product characteristics. 2012. <http://www.medicines.org.uk/emc/medicine/22743/SPC/Synflorix+suspension+for+injection+in+pre-filled+syringe/>. Accessed Sept 29, 2014.
5. Pfizer. Prevenar 13 suspension for injection: summary of product characteristics. 2013. <http://www.medicines.org.uk/emc/medicine/22689/SPC/Prevenar+13+suspension+for+injection/>. Accessed Sept 29, 2014.
6. Butler JC, Schuchat A. Epidemiology of pneumococcal infections in the elderly. *Drugs Aging.* 1999;15(Suppl 1):11–9.
7. Fitzwater S, Chandran A, Santosham M, Johnson H. The worldwide impact of the seven-valent pneumococcal conjugate vaccine. *Pediatr Infect Dis J.* 2012;31:501–8.
8. Weil-Olivier C, van der Linden M, de Schutter I, Dagan R, Mantovani L. Prevention of pneumococcal diseases in the post-seven valent vaccine era: a European perspective. *BMC Infect Dis.* 2012;12:207.
9. Centers for Disease Control and Prevention (CDC). Progress in introduction of pneumococcal conjugate vaccine—worldwide, 2000–2012. *MMWR Morb Mortal Wkly Rep.* 2013;62:308–11.
10. Hanna JN, Humphreys JL, Murphy DM, Smith HV. Invasive pneumococcal disease in non-indigenous people in north Queensland, 2001–2009. *Med J Aust.* 2010;193:392–6.

11. Harboe ZB, Valentiner-Branth P, Benfield TL, et al. Early effectiveness of heptavalent conjugate pneumococcal vaccination on invasive pneumococcal disease after the introduction in the Danish Childhood Immunization Programme. *Vaccine*. 2010;28:2642–7.
12. Miller E, Andrews NJ, Waight PA, Slack MP, George RC. Herd immunity and serotype replacement 4 years after seven-valent pneumococcal conjugate vaccination in England and Wales: an observational cohort study. *Lancet Infect Dis*. 2011;11:760–8.
13. Pilishvili T, Lexau C, Farley MM, et al. Sustained reductions in invasive pneumococcal disease in the era of conjugate vaccine. *J Infect Dis*. 2010;201:32–41.
14. Elston JW, Santaniello-Newton A, Meigh JA, et al. Increasing incidence of invasive pneumococcal disease and pneumonia despite improved vaccination uptake: surveillance in Hull and East Yorkshire, UK, 2002–2009. *Epidemiol Infect*. 2012;140:1252–66.
15. Centers for Disease Control and Prevention (CDC). Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among children aged 6–18 years with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep*. 2013;62:521–4.
16. Centers for Disease Control and Prevention (CDC). Advisory Committee on Immunization Practices (ACIP) recommended immunization schedules for persons aged 0 through 18 years and adults aged 19 years and older—United States, 2013. *MMWR Surveill Summ*. 2013;62 (Suppl 1):1 [Erratum in *MMWR Surveill Summ*. 2013;62:256].
17. Fedson DS, Nicolas-Spony L, Klemets P, et al. Pneumococcal polysaccharide vaccination for adults: new perspectives for Europe. *Expert Rev Vaccines*. 2011;10:1143–67.
18. Huss A, Scott P, Stuck AE, Trotter C, Egger M. Efficacy of pneumococcal vaccination in adults: a meta-analysis. *CMAJ*. 2009;180:48–58.
19. Moberley S, Holden J, Tatham DP, Andrews RM. Vaccines for preventing pneumococcal infection in adults. *Cochrane Database Syst Rev*. 2013;1:CD000422.
20. Maruyama T, Taguchi O, Niederman MS, et al. Efficacy of 23-valent pneumococcal vaccine in preventing pneumonia and improving survival in nursing home residents: double blind, randomised and placebo controlled trial. *BMJ*. 2010;340:c1004.
21. Public Health England. Pneumococcal disease infections caused by serotypes in Prevenar 13 and not in Prevenar 7. 2014. <https://www.gov.uk/government/publications/pneumococcal-disease-caused-by-strains-in-prevenar-13-and-not-in-prevenar-7-vaccine/pneumococcal-disease-infections-caused-by-serotypes-in-prevenar-13-and-not-in-prevenar-7>. Accessed Sept 29, 2014.
22. Picazo J, Ruiz-Contreras J, Casado-Flores J, et al. Expansion of serotype coverage in the universal pediatric vaccination calendar: short-term effects on age- and serotype-dependent incidence of invasive pneumococcal clinical presentations in Madrid, Spain. *Clin Vaccine Immunol*. 2013;20:1524–30.
23. Steens A, Bergsaker MA, Aaberge IS, Ronning K, Vestheim DF. Prompt effect of replacing the 7-valent pneumococcal conjugate vaccine with the 13-valent vaccine on the epidemiology of invasive pneumococcal disease in Norway. *Vaccine*. 2013;31:6232–8.
24. Pradas R, de Gil MA, Alvaro A, et al. Budget impact analysis of a pneumococcal vaccination programme in the 65-year-old Spanish cohort using a dynamic model. *BMC Infect Dis*. 2013;13:175.
25. Boccacini S, Bechini A, Levi M, et al. Cost-effectiveness of new adult pneumococcal vaccination strategies in Italy. *Hum Vaccin Immunother*. 2013;9:699–706.
26. ClinicalTrials.gov. Study evaluating the efficacy of a 13-valent pneumococcal conjugate vaccine (13vPnC) in adults (CAPITA). 2014. <http://www.clinicaltrials.gov/ct2/show/NCT00744263?term=Prevenar+13&rank=92>. Accessed Sept 29, 2014.
27. Hak E, Grobbee DE, Sanders EA, et al. Rationale and design of CAPITA: a RCT of 13-valent conjugated pneumococcal vaccine efficacy among older adults. *Neth J Med*. 2008;66:378–83.
28. Bundesministerium für gesundheit. Österreichischer Impfplan 2014. 2014. [http://bmg.gv.at/home/Schwerpunkte/Praevention/Impfen/Oesterreichischer\\_Impfplan\\_2014](http://bmg.gv.at/home/Schwerpunkte/Praevention/Impfen/Oesterreichischer_Impfplan_2014). Accessed Sept 29, 2014.
29. Conseil Supérieur de la Santé. Vaccination antipneumococcique: vaccination de l'adulte (révision 13). 2013. [http://www.health.belgium.be/filestore/19086989\\_FR/vaccination%20fiche%20contre%20pneumococque.pdf](http://www.health.belgium.be/filestore/19086989_FR/vaccination%20fiche%20contre%20pneumococque.pdf). Accessed Sept 29, 2014.
30. Conseil Supérieur de la Santé. Recommandations pour la vaccination des enfants présentant un risque accru de maladie invasive à pneumocoques (révision 13). 2013. <http://www.health.belgium.be/>

- [filestore/19076834\\_FR/fiche%20de%20vaccination%208757%2016012013.pdf](filestore/19076834_FR/fiche%20de%20vaccination%208757%2016012013.pdf). Accessed Sept 29, 2014.
31. Statens Serum Institut. Pneumococcal vaccination of persons at increased risk of invasive pneumococcal disease. 2012. <http://www.ssi.dk/English/News/EPI-NEWS/2012/No%2051b%20-%202012.aspx>. Accessed Sept 29, 2014.
  32. Terveiden ja hyvinvoinnin laitos. Pneumokokkirokotukset. 2013. [http://www.thl.fi/fi\\_FI/web/rokottajankasikirja-fi/pneumokokkirokotukset](http://www.thl.fi/fi_FI/web/rokottajankasikirja-fi/pneumokokkirokotukset). Accessed Sept 29, 2014.
  33. Haut Conseil de la Santé Publique. Infections invasives à pneumocoque : recommandations vaccinales pour les personnes à risque. 2013. <http://www.hcsp.fr/Explore.cgi/avisrapportsdomaine?clefr=355>. Accessed Sept 29, 2014.
  34. Ständigen Impfkommision am Robert Koch-Institut (RKI). Empfehlungen der Ständigen Impfkommision (STIKO) am Robert Koch-Institut/Stand: August 2014. [http://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2014/Ausgaben/34\\_14.pdf?\\_\\_blob=publicationFile](http://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2014/Ausgaben/34_14.pdf?__blob=publicationFile). Accessed Sept 29, 2014.
  35. Der Sächsischen Impfkommision. Empfehlungen der Sächsischen Impfkommision zur Durchführung von Schutzimpfungen im Freistaat Sachsen. 2014. [http://www.gesunde.sachsen.de/download/lu/LUA\\_HM\\_Impfempfehlungen\\_E1.pdf](http://www.gesunde.sachsen.de/download/lu/LUA_HM_Impfempfehlungen_E1.pdf). Accessed Sept 29, 2014.
  36. Διεύθυνση Δημόσιας Υγείνης του Υπουργείου Υγείας και Κοινωνικής Αλληλεγγύης. Εθνική Επιτροπή Εμβολιασμών. Πρόγραμμα Εμβολιασμών Ενηλίκων (Αθήνα 21/12/2011, Αρ Πρωτ. Υ1/Γ.Π.οικ.140958). Available: <http://static.diavgeia.gov.gr/doc/45%CE%A8%CE%A8%CE%98-2%CE%98%CE%9C>. Accessed Sept 29, 2014.
  37. National Immunisation Advisory Committee of the Royal College of Physicians of Ireland. Immunisation Guidelines for Ireland, 2013 Edition (updated June 2014); Chapter 16, pneumococcal infection. 2013. <http://www.immunisation.ie/en/HealthcareProfessionals/ImmunisationGuidelines/>. Accessed Sept 29, 2014.
  38. Regione Basilicata. Circolare Regione Basilicata del 5.11.2012 Prot. N. 194806/72AF. 2012. <http://www.regione.basilicata.it/giunta/site/giunta/detail.jsp?otype=1012&id=602510>. Accessed Sept 29, 2014.
  39. Provincia Autonoma di Bolzano. Recepimento dell'accordo Stato—Regioni e Province autonome di Trento e Bolzano del 22.02.2012 n. 54—Piano Vaccinale. Delibera della Giunta Provinciale n.693 del 13.5.2013. 2013. <http://www.regione.taa.it/bur/pdf/I-II/2013/21/S1/S121130184418.pdf>. Accessed Sept 29, 2014.
  40. Dipartimento di Prevenzione ASL Cagliari. Circolare Dipartimento di Prevenzione ASL Cagliari del 17.11.2011 Prot. N. 16043. 2011.
  41. Regione Emilia Romagna Direzione Generale della Sanità—Servizio Sanità Pubblica. Aggiornamento delle indicazioni sulle vaccinazioni per la prevenzione delle malattie invasive batteriche nelle persone con patologie o condizioni di rischio. PG 2014/240655 del 19.06.2014. 2014. [http://www.saluter.it/documentazione/leggi/regionali/comunicazioni/malattie\\_batteriche\\_indicazioni\\_2014.pdf/view](http://www.saluter.it/documentazione/leggi/regionali/comunicazioni/malattie_batteriche_indicazioni_2014.pdf/view). Accessed Sept 29, 2014.
  42. Consiglio Regionale Del Friuli Venezia Giulia. Estensione dell'offerta vaccinale nella regione FVG. 2012. <http://www.medicoeleggi.com/argomenti02/fvg/bur/600929.htm>. Accessed Sept 29, 2014.
  43. Regione Lazio Dipartimento Programmaz Economica E Sociale. Approvazione del bando di concorso pubblico regionale straordinario per titoli per l'assegnazione delle sedi farmaceutiche disponibili per il privato esercizio nella Regione Lazio N. 63 del 13/11/2012. Bollettino Ufficiale Della Regione Lazio 2012. [http://www.regione.lazio.it/binary/rl\\_main/tbl\\_concorsi/2012\\_6681.pdf](http://www.regione.lazio.it/binary/rl_main/tbl_concorsi/2012_6681.pdf). Accessed Sept 29, 2014.
  44. Regione Liguria DSeSsPSP. Fasce deboli Sicurezza alimentare e Sanità animale. Prevenzione della Malattia pneumococcica negli adulti con età superiore a 64 anni e nei giovani ed adulti con fattori di rischio—istruzioni operative. Prot. 11235 del 21.1.2013. 2013.
  45. Regione Lombardia ASL Milano. Indicazioni vaccinazione antipneumococco nell'adulto e nell'anziano del 10/01/2011. 2011.
  46. La Regione Marche Segreteria della Giunta regionale. Deliberazione n. 480 del 03/04/2013: Recepimento del piano nazionale prevenzione vaccinale 2012-2014. Bollettino Ufficiale Della Regione Marche 2013;N. 29:6186-209. [http://213.26.167.158/bur/PDF/13/N29\\_22\\_04\\_2013.pdf](http://213.26.167.158/bur/PDF/13/N29_22_04_2013.pdf). Accessed Sept 29, 2014.
  47. Regione Piemonte. Circolare Regione Piemonte Prot. N. 7189/DB2017 del 07.03.2013. 2013.
  48. Regione Puglia. Circolare Regione Puglia Prot. AOO152/13 Marzo 2012/n. 3731. 2012.
  49. Ufficio legislativo e legale della Regione Siciliana. N. 23 del 08/06/2012. Gazzetta Ufficiale Della Regione Siciliana 2012. <http://www.gurs.regione.sicilia.it/>



- [Gazzette/g12-23/g12-23.pdf](#). Accessed Sept 29, 2014.
50. Provincia Autonoma Di Trento, Servizio organizzazione e qualità delle attività sanitari. Piano provinciale di promozione delle vaccinazioni per la provincia di Trento. 2012. <http://www.epicentro.iss.it/temi/vaccinazioni/pdf/Normative/Trentino%20Alto%20Adige/Trentino,%20Trento%20-%20Dicembre%202012/PPPVPT%2012-14%20DGR%20n%C2%B0%2017%20del%2013.01.2012%20Testo.pdf>. Accessed Sept 29, 2014.
  51. Azienda USL 7 Siena -Dipartimento di Prevenzione—Igiene e sanità pubblica. Direttiva ai Medici di Medicina Generale. April 2012. 2012.
  52. Regione Umbria Giunta Regionale. Deliberazione Della Giunta Regionale N. 607 Del 28/05/2012: Recepimento del “Piano nazionale per l’eliminazione del morbillo e della rosolia congenita (PNEMoRc) 2010-2015” e del “Piano Nazionale Prevenzione Vaccinale 2012-2014” e integrazione del Protocollo regionale delle vaccinazioni raccomandate di cui alla DGR n. 84/2008. 2012. [http://www.epicentro.iss.it/temi/vaccinazioni/pdf/Normative/Umbria\\_Maggio%202012/PNPV%2012-14%20+%20PNEMoRc%2010-15%20%20DGR%20n%C2%B0%20607%20del%202012.pdf](http://www.epicentro.iss.it/temi/vaccinazioni/pdf/Normative/Umbria_Maggio%202012/PNPV%2012-14%20+%20PNEMoRc%2010-15%20%20DGR%20n%C2%B0%20607%20del%202012.pdf). Accessed Sept 29, 2014.
  53. Federazione Italiana Medici Pediatri Veneto. Prevenzione delle malattie batteriche invasive nei Soggetti con asplenia anatomica o funzionale e altre condizioni di rischio. 2012. <http://www.fimp.veneto.it/sites/default/files/Calendario%20Vaccinale%20e%20Categorie%20a%20Rischio%202012.pdf>. Accessed Sept 29, 2014.
  54. Ministero Della Salute. Piano Nazionale Vaccini 2005-2007. 2005. [http://www.salute.gov.it/portale/documentazione/p6\\_2\\_2\\_1.jsp?lingua=italiano&id=543](http://www.salute.gov.it/portale/documentazione/p6_2_2_1.jsp?lingua=italiano&id=543). Accessed Sept 29, 2014.
  55. Conseil Superieur D’hygiene. Recommendations pour la vaccination contre le pneumocoque par le vaccin 23 valent. 2008. <http://www.sante.public.lu/fr/recommandations/conseil-maladies-infectieuses/pneumonie/recommandations-vaccinations-2008/pneumonie-recommandations-vaccinatin-pneumo-coque-23valent-2008.pdf>. Accessed Sept 29, 2014.
  56. Conseil Superieur D’hygiene. Vaccination universelle des nourrissons et des enfants contre les infections invasives à *Streptococcus pneumoniae*—mise à jour 2011. 2011. <http://www.sante.public.lu/fr/recommandations/conseil-maladies-infectieuses/pneumonie/recommandations-vaccinations-2011/2011-02-vaccination-nourrissons-streptococcus-pneumoniae.pdf>. Accessed Sept 29, 2014.
  57. Rijksinstituut voor Volksgezondheid en Milieu. Richtlijn voor preventie van infecties bij mensen met (functionele) hypo- en asplenie. 2012. [http://www.rivm.nl/dsresource?objectid=rivmp:52820&type=org&disposition=inline&ns\\_nc=1](http://www.rivm.nl/dsresource?objectid=rivmp:52820&type=org&disposition=inline&ns_nc=1). Accessed Sept 29, 2014.
  58. Helse- og omsorgsdepartementet. Forskrift om stønad til dekning av utgifter til viktige legemidler mv. (blåreseptforskriften). 2007. <http://www.lovdata.no/for/sf/ho/xo-20070628-0814.html>. Accessed Sept 29, 2014.
  59. Nasjonalt folkehelseinstitutt. Anbefalinger for bruk av pneumokokkvaksine utenfor barnevaksinasjonsprogram i Norge. 2013. <http://www.fhi.no/dokumenter/14a5077fef.pdf>. Accessed Sept 29, 2014.
  60. Direcção-Geral da Saúde. Vacinação, a nível hospitalar, contra infecções por *Streptococcus pneumoniae* de crianças/adolescentes de risco para doença invasiva pneumocócica (DIP). 2010. <http://www.dgs.pt/upload/membro.id/ficheiros/i013057.pdf>. Accessed Sept 29, 2014.
  61. Ministerio de Sanidad SSeI. Pfizer data on file. 2012.
  62. Agència de Salut Pública de Catalunya. Prevenció de la malaltia pneumocòccica en els adults i en els infants a partir dels 5 anys a Catalunya. 2014. [http://www2.gencat.cat/docs/canalsalut/Home%20Canal%20Salut/Professionals/Temes\\_de\\_salut/Vacunacions/documents/Arxius/Prevencio\\_neumo\\_Catalunya\\_adults.pdf](http://www2.gencat.cat/docs/canalsalut/Home%20Canal%20Salut/Professionals/Temes_de_salut/Vacunacions/documents/Arxius/Prevencio_neumo_Catalunya_adults.pdf). Accessed Sept 29, 2014.
  63. Xunta De Galicia Consellería De Sanidade. Instrución: sobre a utilización da vacina antipneumocócica conxugada trecevalente en persoas de 50 ou máis anos pertencentes a grupos de risco. 2012. [http://www.sergas.es/gal/DocumentacionTecnica/docs/SaudePublica/vacunas/PNEUMO\\_conxugada\\_adultos\\_firmada.pdf](http://www.sergas.es/gal/DocumentacionTecnica/docs/SaudePublica/vacunas/PNEUMO_conxugada_adultos_firmada.pdf). Accessed Sept 29, 2014.
  64. Región de Murcia, Dirección General de Salud Pública. Vacuna antineumocócica conjugada en personas de 6 o más años. Indicaciones de dispensación gratuita. 2014. [http://www.murciasalud.es/recursos/ficheros/245766-febrero\\_2014.pdf](http://www.murciasalud.es/recursos/ficheros/245766-febrero_2014.pdf). Accessed Sept 29, 2014.
  65. Colegio Oficial de Enfermería de Gipuzkoa. Vacunación. Suministro de Vacunas para grupos de riesgo en la CAPV. 2013. <http://www.coegi.org/Contenidos/Ficha.aspx?IdMenu=09870026-02f2-4de1-b6b5-4d1b087c2bdd>. Accessed Sept 29, 2014.
  66. Dirección General de Salud Pública, Generalitat Valenciana Conselleria De Sanitat. Instrucción: sobre la utilización de vacuna antineumocócica

- 
- conjugada trecevalente en personas de 18 o más años pertenecientes a grupos de riesgo. 2013. [http://www.sp.san.gva.es/DgspPortal/docs/instruccionesdevacunacion\\_18anyos\\_11nov\\_2013.pdf](http://www.sp.san.gva.es/DgspPortal/docs/instruccionesdevacunacion_18anyos_11nov_2013.pdf). Accessed Sept 29, 2014.
67. Servicio Madrileño De Salud, Dirección General De Atención Primaria. Instrucción sobre vacunación frente al neumococo en la comunidad de Madrid. 2013. [http://www.madrid.org/cs/Satellite?c=PTSA\\_Multimedia\\_FA&cid=1354263566935&pagename=PortalSalud%2FPPTSA\\_Multimedia\\_FA%2FPPTSA\\_documentoWebeditpro](http://www.madrid.org/cs/Satellite?c=PTSA_Multimedia_FA&cid=1354263566935&pagename=PortalSalud%2FPPTSA_Multimedia_FA%2FPPTSA_documentoWebeditpro). Accessed Sept 29, 2014.
68. Instituto De Salud Pública De Navarra. Instrucciones sobre la vacunación de adultos y en situaciones clínicas especiales. 2013. <http://www.navarra.es/NR/rdonlyres/AECCD760-AB2A-4841-818A-FA53478FD6DC/255921/BOL72INT.pdf>. Accessed Sept 29, 2014.
69. Servicio Extremeño de Salud. Programa de Vacunaciones. protocolo de gestión de vacunas (Marzo de 2013). Servicio Extremeño de Salud. 2013.
70. Ministerio De Sanidad Y Consumo. Vacunación en Adultos: Recomendaciones Año 2004. 2004. <http://www.msssi.gob.es/ciudadanos/proteccionSalud/vacunaciones/docs/recoVacunasAdultos.pdf>. Accessed Sept 29, 2014.
71. Janusinfo Stockholms Läns Landsting. Konjugatvaccin i kombination med polysackaridvaccin för vaccination av barn från 2 års ålder och vuxna med stor risk för att drabbas av pneumokockinfektion. 2013. <http://www.janusinfo.se/Behandling/Expertradsutlatanden/Vaccinationer/Konjugatvaccin-for-vaccination-av-barn-aldre-an-5-ar-och-vuxna-med-stor-risk-for-att-drabbas-av-pneumokockinfektion>. Accessed Sept 29, 2014.
72. Socialstyrelsen. SOSFS 1994:26; Socialstyrelsens allmänna råd; Vaccination mot pneumokocker. 1994. <http://www.socialstyrelsen.se/publikationer/1994/1994-10-26>. Accessed Sept 29, 2014.
73. Public Health England. Pneumococcal: the green book, chapter 25. 2013. <https://www.gov.uk/government/publications/pneumococcal-the-green-book-chapter-25>. Accessed Sept 29, 2014.