

COMMUNICATIONS C24  
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## Antimeningococcal and antipneumococcal vaccination determinants: a European systematic literature review

Analisi dei determinanti associati con la vaccinazione antimeningococco C e antipneumococco: risultati di una revisione sistematica di letteratura condotta in Europa

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### Abstract

**Background.** ESCULAPIO is a multicenter project, funded by the Italian Centre for Disease Prevention and Control, aimed at implementing communication strategies to improve vaccination knowledge and attitudes among different target populations.

**Objective.** The objective of the Sicilian research unit was, in the first phase, to identify, through systematic literature revision, which vaccination determinants play a role in the uptake of recommended vaccines included in the Italian Vaccination Plan.

**Design.** A systematic literature review was carried out on studies describing the determinants underlying pneumococcal and meningococcal vaccination uptake. The analysis was limited to papers published in English from 2000 to date.

**Results.** A total of 188 (meningococcal) and 731 (pneumococcal) papers were found. After selection by publication data, country (Europe), article type (original article), target population (healthy subjects), 7 (meningococcal) and 4 (pneumococcal) manuscripts were finally included in the analysis. For meningococcal vaccination a better socioeconomic status is related to vaccination acceptance, whereas distance from immunization service is a negative determinant. For pneumococcal vaccination the determinants related to vaccination uptake are older parental age and a strong vaccine recommendation. Conversely, when the vaccine needs to be paid for, a refusal is more likely

**Conclusions.** Our results show that payment for vaccination is a major barrier and communication about meningococcal and pneumococcal vaccination should be targeted towards specific population groups, especially through the counseling activities by health professionals.

(*Epidemiol Prev* 2015; 39(4) Suppl 1: 59-64)

**Key words:** systematic literature review, meningococcal vaccination, pneumococcal vaccination

### Riassunto

**Introduzione.** ESCULAPIO è un progetto multicentrico, finanziato dal Centro per la prevenzione e il controllo delle malattie, che ha tra i suoi obiettivi quello di sviluppare strategie per implementare le conoscenze vaccinali in differenti target di popolazione.

**Obiettivi.** L'U.O. della Sicilia aveva il compito di identificare i determinanti associati con l'adesione vaccinale delle vaccinazioni raccomandate presenti nel Piano nazionale vaccini.

**Disegno.** Sono state condotte due revisioni sistematiche di letteratura sui determinanti associati con le vaccinazioni anti-meningococco e anti-pneumococco.

**Risultati.** Attraverso le stringhe di ricerca specifiche sono stati trovati 188 (meningococco) e 731 (pneumococco) articoli. Selezionando per data di pubblicazione (dal 2000 a oggi), nazione (Europa), tipologia di articolo (articoli originali), popolazione target (no soggetti a rischio), sono stati inclusi nell'analisi 7 (meningococco) e 4 (pneumococco) lavori. Per il meningococco il principale fattore pro-vaccinazione è un migliore status socioeconomico, mentre la distanza dai servizi vaccinali è un determinante negativo. I determinanti associati con la vaccinazione antipneumococcica sono una maggiore età dei genitori e la raccomandazione alla vaccinazione da parte dell'operatore sanitario. Viceversa, il pagamento del vaccino implica un rifiuto vaccinale.

**Conclusioni.** I risultati dimostrano che il pagamento della vaccinazione costituisce una barriera fondamentale e che gli sforzi informativi/comunicativi in tema vaccinale devono essere rivolti prevalentemente alle fasce di popolazione che necessitano di un maggiore supporto, specialmente attraverso l'attività di counselling vaccinale da parte dell'operatore sanitario di riferimento.

(*Epidemiol Prev* 2015; 39(4) Suppl 1: 59-64)

**Parole chiave:** revisione sistematica di letteratura, vaccinazione antipneumococcica, vaccinazione antimeningococcica

## BACKGROUND

In 2012, the Italian Centre for Disease Prevention and Control (CCM) of the Ministry of Health, funded a multicenter research project presented by researchers of six Italian regions (Toscana: leading proponent; Liguria, Puglia, Sardegna, Sicilia, Veneto) entitled *Development of health communication strategies and interventions on preventable diseases and vaccination to increase vaccine coverage in the general population*. For every region, a research unit constituted by researchers from universities or Local Public Health authorities was identified, with specific population targets. The project was finally renamed with the acronym ESCULAPIO. The target for the Sicilian research unit was the evaluation of the determinants related with vaccination uptake among the general population. In particular, in a first phase of the study, the Sicilian Unit conducted systematic literature reviews (SLR) for the most important optional vaccinations recommended by the Italian National Vaccination Plan (*Human papillomavirus*, influenza, measles, mumps and rubella, meningococcal, pneumococcal).<sup>1</sup>

In this manuscript, data on studies describing the determinants underlying pneumococcal and meningococcal vaccination uptake among the general population are reported.

### Meningococcal vaccination

Meningococcal vaccination is a relatively recent public health acquisition. Despite meningococcal polysaccharide vaccines having been available for several decades, effectiveness was not satisfactory.<sup>2</sup> The first conjugate vaccine against *Neisseria meningitidis* serogroup C was approved only in 1999.<sup>2</sup> In the following years, the introduction of the quadrivalent conjugate vaccine against *Neisseria meningitidis* serogroups A, C, W135, and Y improved the vaccination offer. Nevertheless, for many years the meningococcal quadrivalent vaccine was recommended only for some groups of the population, according to socio-occupational (e.g., soldiers, males who have sex with males, travelers in high risk areas) or clinical (e.g., thalassemia, asplenia, chronic liver disease, chronic renal failure, AIDS) characteristics.<sup>3</sup> Only in 2014, recommendations for quadrivalent meningococcal vaccination was extended for routine infant vaccination (<2 years old).<sup>4</sup> Moreover, in 2013 a vaccine against *Neisseria meningitidis* serogroup B in infants was finally licensed.<sup>5</sup> Therefore, in the international scientific literature, determinants associated with meningococcal A, B, W135, and Y serogroups vaccination were not analyzed, limiting available data to meningococcal C vaccination.<sup>6-12</sup>

### Pneumococcal vaccination

The history of pneumococcal vaccination began more than 30 years ago in the USA, where the 23-valent pneumococcal polysaccharide vaccine (PPSV23) was licensed. Nowadays, PPSV23 is currently recommended in people aged  $\geq 65$  years and in high-risk adults aged 19-64 years.<sup>13</sup> However, PPSV23 has limited effectiveness against invasive pneumococcal disease, especially among immunocompromised adults, and PPSV23 protection is short-lived, with a rapid waning of antibody concentrations and with a lack of memory B-cell production following immunization.<sup>14-16</sup>

Since 2000, the offer of pneumococcal vaccine has been enriched by a conjugate 7-valent vaccine (PCV7) for all children aged 2-23 months.<sup>17</sup> In 2010, PCV7 vaccine was replaced by a 13-valent vaccine (PCV13) with six additional serotypes.<sup>13-18</sup> Both conjugate vaccinations demonstrated good efficacy and effectiveness in invasive pneumococcal disease (IPD) prevention.<sup>19-20</sup>

On August 2014, the Advisory Committee on Immunization Practices (ACIP) recommended routine use of PCV13 even among adults aged  $\geq 65$  years, extending the vaccine indication to community-acquired pneumonia.<sup>13</sup>

## MATERIAL AND METHODS

An SLR was carried out on determinants associated with meningococcal and pneumococcal vaccination compliance, considering key terms used in combination and referred to vaccine/immunization, uptake/coverage, determinant/factor, and *Neisseria meningitidis*/meningococcal/meningococcus or *Streptococcus pneumoniae*/pneumococcus/pneumococcal, with medical subject headings (MeSH) and MeSH major topics included in the syntax. The PubMed/MEDLINE, SCOPUS, EMBASE, and ISI Web of Science online databases were considered, as well as the grey literature, and a manual search was performed based on the references of the articles retrieved. Original articles published from January 2000 to December 2014 were collected (figure 1).

Qualitative and quantitative studies describing the determinants underlying meningococcal or pneumococcal vaccination uptake among parents of children or adolescents/adults were included in the review. Exclusion criteria applied during title and abstract screening were: articles published in a language different from English, Italian, or French, studies conducted in non-European countries, studies reporting vaccination information on non-healthy populations, studies other than original articles (e.g., review) (figure 1). Other exclusion criteria were applied during full text analysis: assessing only vaccination coverage; reporting uptake determinants not in first person or not by parents; not reporting direct linking with uptake (e.g., linking with adverse publicity or with information-seeking) (figure 1).

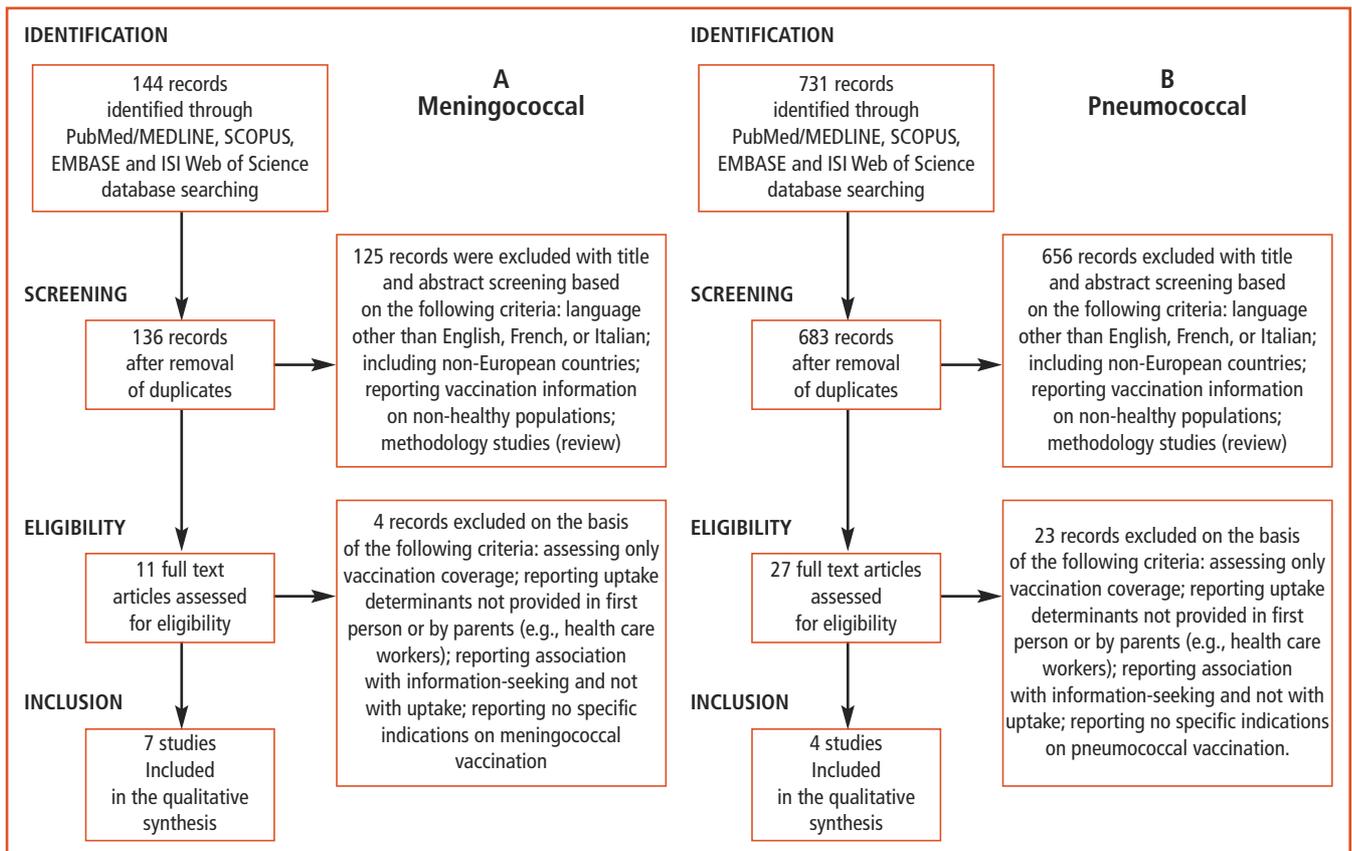
Variable extraction was conducted on the basis of potential classes of determinants identified in previous SLRs, that included among others: knowledge, beliefs, and perceptions (both on vaccines and diseases); attitudes/behaviours; demographics (such as ethnicity, mother's age, child's age, gender, geographic location); socioeconomic status (SES) (including education level, employment, family income, number of children in the household).<sup>21</sup>

The literature search and systematic review were conducted by two independent investigators. In case of any incongruity, the two investigators came to an agreement after further analysis and discussion.

## RESULTS

### Meningococcal vaccination

As shown in figure 1, through the standardized database searching, 144 records were identified. After duplicates were removed, 135 records were screened and 125 records were excluded on the basis of title and abstract screening (based on language, study setting, methodology, or target population).



**Figure 1.** Flow SLR diagram of the determinants of pneumococcal (A) and meningococcal (B) vaccination.

**Figura 1.** Diagramma di flusso delle RSL relative ai determinanti delle vaccinazioni antimeningococco (A) e antipneumococco (B).

Finally, among 11 articles assessed for eligibility, 4 were excluded on basis of exclusion criteria and 7 were analyzed in the qualitative synthesis.

Manuscripts included in the meningococcal vaccination SLR are summarized in [table 1](#).

In particular, the first European experience analyzing vaccine status and determinants of British undergraduates in South Wales (mean age in years 18.9, 51% females), showed that the supply of meningococcal C vaccination through school-based campaigns (93% vaccinated *vs* 19% vaccinated without an active vaccination offer) was the most important determinant for vaccination acceptance.<sup>6</sup>

A study conducted in 2005 among 1,763 Dutch parents of children aged 6 to 14 years old demonstrated that ethnicity, religion (not practicing), and a higher parent education level were related with vaccination acceptance.<sup>7</sup>

Vaccination coverage (VC) reported in the study was 84%. Considering the diversity of the Dutch population, analysis of the different ethnicities showed there was better information, risk awareness, and critical attitudes towards meningococcal vaccination among Dutch parents compared to parents of different ethnicity (e.g., Turkish, Moroccan, Surinamese).<sup>7</sup>

Perceptions, attitudes, and behaviour regarding meningococcal vaccination were also analyzed in the Netherlands among the same group of parents.<sup>9</sup> Specifically, a higher perceived vulnerability of their own child contracting meningococcal disease and

a perceived control of vaccination in preventing meningococcal C infection were strongly related with vaccination acceptance.<sup>9</sup> In 2005, a retrospective study conducted in Belgium (EPI-survey), reported coverage and predictive factors associated with childhood vaccination compliance. In particular, for meningococcal vaccination (VC=94%), using the paediatrician as a referent for vaccination counselling in the multivariate analysis, a better vaccination attitude was shown to be related with “well-baby clinic” or “daycare” vaccination counseling (OR 1.9; 95%CI 1.2-2.8).<sup>8</sup> Conversely, a family physician vaccination counseling represents a barrier for meningococcal vaccination (OR 0.4; 95%CI 0.2- 0.8).<sup>8</sup>

Results of the EPI-survey study among parents of 14- and 7-year-old Belgian children were also reported.<sup>10-11</sup> In particular, among 14-year-old children, the determinants associated with vaccination uptake were mother’s education (secondary school or higher: OR 1.7; 95%CI 1.0-2.9) and employment (part-time work: OR 1.9; 95%CI 1.4-2.7), whereas the determinants associated with vaccination refusal were the adolescent’s school career (repeated 1 year: OR 0.6; 95%CI 0.4-0.8; special education: OR 0.4; 95%CI 0.2-0.7), mother’s ethnicity (non European: OR 0.4; 95%CI 0.3-0.7), and father’s employment (part-time work: OR 0.2; 95%CI 0.0-0.8).<sup>10</sup>

Among parents of 7-year-old children, vaccination uptake was strongly related with higher family income (>€3,000/month: OR 2.92; 95%CI 1.39-6.09).<sup>11</sup>

Finally, a cross-sectional survey conducted in Poland among parents of 0-5 years olds children highlighted lower meningococcal VC than the Netherlands and Belgium.<sup>12</sup>

Vaccination compliance was related with older parental age (>25 years: OR 2.60; 95%CI 1.03-6.83), higher socio-economic status of the family (OR 3.46; 95%CI 1.95-8.48), number of children (one: OR 3.64; 95%CI 1.96-7.14), and area of family physician practice (town: OR 3.94; 95%CI 1.95-8.48).<sup>12</sup> High cost of the vaccine was associated with vaccination refusal (OR 0.18; 95%CI 0.09-0.36).<sup>12</sup>

### Pneumococcal vaccination

For pneumococcal vaccination, 731 records were identified through the database search (figure 1). After duplicates were removed, 683 records were screened and 656 records were excluded on the basis of title and abstract screening (based on lan-

guage, study setting, methodology or target population). Finally, among 27 articles assessed for eligibility, 23 were excluded on the basis of the exclusion criteria and 4 were analyzed in the qualitative synthesis. Manuscripts included in the pneumococcal vaccination SLR are summarized in table 2.<sup>12,22-24</sup>

The first article analyzed was a survey conducted in 2002 on a sample of adults ≥65 years of age conducted in 11 Italian regions.<sup>22</sup> Vaccination coverage reported for PPSV23 was only 5%. Factors associated with vaccination uptake were a strong recommendation by the family general practitioner (GP), free-of-charge vaccination, and perception of the danger of pneumococcal disease.<sup>22</sup>

In 2009, a cross-sectional study was conducted among parents of 0-5 year old Polish children to measure coverage and determinants of self-paid vaccinations.<sup>12</sup> Factors associated with PCV7 pneumococcal vaccination uptake were the same as

Manuscript (1 <sup>st</sup> author, journal, publication date)	Geographical setting/ target population	Adolescents (own vaccination)		Parents (vaccination on their child)		Type of determinant
		facilitator	barrier	facilitator	barrier	
Thirlaway K <sup>6</sup> <i>Commun Dis Public Health</i> 2003	UK undergraduates (18-21 years old)	<ul style="list-style-type: none"> <li>■ UK residence</li> <li>■ living in student accommodation</li> <li>■ school-based vaccination program</li> </ul>	Irish residence			<ul style="list-style-type: none"> <li>■ demographic factors (residence)</li> <li>■ socio-economic factors (accommodation type)</li> <li>■ vaccination strategies</li> </ul>
Timmermans D et al. <sup>7</sup> <i>Vaccine</i> 2005	Netherlands parents of children 6-14 years old			<ul style="list-style-type: none"> <li>■ ethnicity (Dutch);</li> <li>■ religion (not practicing)</li> <li>■ higher parental education level</li> </ul>		<ul style="list-style-type: none"> <li>■ demographic factors (ethnicity, religion)</li> <li>■ parents' education level</li> </ul>
Theeten H et al. <sup>8</sup> <i>Vaccine</i> 2007	Belgium parents of children 18-24 months			main vaccinating physician: well-baby clinic or daycare (referent: pediatrician)	main vaccinating physician: family physician (referent: pediatrician)	type of health care workers recommending vaccination
Timmermans D et al. <sup>9</sup> <i>BMC Public Health</i> 2008	Netherlands parents of children 6-14 years old			<ul style="list-style-type: none"> <li>■ perceived vulnerability of their own child</li> <li>■ perceived control in preventing meningococcal infection</li> </ul>	psychosocial factors	(perceptions, attitudes, and behaviours)
Vandermeulen C et al. <sup>10</sup> <i>Pediatrics</i> 2008	Belgium parents of adolescents 14 years old	school career of adolescent (repeated 1 year, special education)		<ul style="list-style-type: none"> <li>■ higher mother's education</li> <li>■ mother's employment (part-time work)</li> </ul>	<ul style="list-style-type: none"> <li>■ race of the mother (non European)</li> <li>■ father's employment (part-time work)</li> </ul>	<ul style="list-style-type: none"> <li>■ demographic factors (race)</li> <li>■ education level (parents)</li> <li>■ employment type (parents)</li> <li>■ education-related factors (adolescent)</li> </ul>
Theeten H et al. <sup>11</sup> <i>Acta Paediatr</i> 2009	Belgium parents of children 7 years old			higher socioeconomic status (family income)		socioeconomic factors (family income)
Ganczak M et al. <sup>12</sup> <i>Vaccine</i> 2013	Poland parents of children 0-5 years old			<ul style="list-style-type: none"> <li>■ age ≥25 years old</li> <li>■ number of children in the family (one)</li> <li>■ higher socioeconomic status (family income)</li> <li>■ area of family physician practice (town)</li> </ul>	<ul style="list-style-type: none"> <li>■ number of children in the family (more than one)</li> <li>■ high cost of the vaccine</li> </ul>	<ul style="list-style-type: none"> <li>■ demographic factors (parents' age, number of children)</li> <li>■ socioeconomic factors (family income)</li> <li>■ family physician related factors (area of practice)</li> <li>■ cost of the vaccine</li> </ul>

**Table 1.** Determinants for meningococcal vaccination reported in the manuscripts included in the systematic literature review.

**Tabella 1.** Determinanti associati con la vaccinazione antimeningococcica inclusi negli articoli della revisione sistematica di letteratura.

Manuscript (1 <sup>st</sup> author, journal, publication date)	Geographical setting; target population	Adolescents (own vaccination)		Parents (vaccination on their child)		Type of determinant
		facilitator	barrier	facilitator	barrier	
Sammarco S et al. <sup>22</sup> <i>Annali di Igiene</i> 2004	Italy people aged ≥65 years old	<ul style="list-style-type: none"> <li>■ strong vaccine recommendation</li> <li>■ free vaccination</li> <li>■ perceived dangerous disease</li> </ul>				<ul style="list-style-type: none"> <li>■ psychosocial factors (perceptions, attitudes, and behaviours)</li> <li>■ vaccination strategies</li> </ul>
Ganczak M et al. <sup>12</sup> <i>Vaccine</i> 2013	Poland parents of children 0-5 years old			<ul style="list-style-type: none"> <li>■ age ≥25 years</li> <li>■ number of children in the family (one)</li> <li>■ higher socioeconomic status (family income)</li> </ul>	<ul style="list-style-type: none"> <li>■ high cost of the vaccine</li> </ul>	<ul style="list-style-type: none"> <li>■ demographic factors (parents' age, family composition)</li> <li>■ socioeconomic factors (family income)</li> <li>■ family physician related factors (area of practice)</li> <li>■ cost of the vaccine</li> </ul>
Lode H et al. <sup>23</sup> <i>Advances in Therapy</i> 2013	13 Western European countries adults aged >50 years	<ul style="list-style-type: none"> <li>■ perception of vaccine efficacy and effectiveness</li> <li>■ health care worker recommendation</li> </ul>	<ul style="list-style-type: none"> <li>■ lack of physician recommendations</li> <li>■ vaccine awareness</li> <li>■ not being concerned about pneumococcal infections</li> </ul>			<ul style="list-style-type: none"> <li>■ psychosocial factors (perceptions, attitudes, and behaviours)</li> </ul>
Robert E et al. <sup>24</sup> <i>BioMed Research Intern</i> 2014	Belgium parents of children aged 18-24 months			<ul style="list-style-type: none"> <li>■ attending Mother &amp; Child clinics or a daycare</li> <li>■ number of children</li> </ul>		<ul style="list-style-type: none"> <li>■ vaccination strategies</li> <li>■ demographic factors (number of children) in the family (one)</li> </ul>

**Table 2.** Determinants for pneumococcal vaccination reported in the manuscripts included in the systematic literature review.

**Tabella 2.** Determinanti associati con la vaccinazione antipneumococcica inclusi negli articoli della revisione sistematica di letteratura.

those reported above for meningococcal vaccination.<sup>12</sup> A multicenter survey carried out in 13 Western European countries investigated attitudes to vaccination in people aged >50 years.<sup>23</sup> As reported in **table 2**, the principal determinants for pneumococcal vaccination uptake were perception of vaccination efficacy and effectiveness and a strong recommendation from the GP. Similarly, factors associated with vaccine refusal were: lack of physician recommendation or vaccine awareness, and not being concerned about pneumococcal infections.

Finally, the results of two cross-sectional studies performed in 2012 in two Belgian regions among parents of 18-24 months-old children were reported.<sup>24</sup>

The predictor most often and most strongly associated with PCV7 vaccination was Mother and Child clinic attendance (Wallonia region: OR 2.8; 95%CI 1.5-5.1; Brussels-Capital region: OR 4.8; 95%CI 2.4-9.4).<sup>24</sup> In Wallonia, having only one child was related with higher vaccination uptake (OR 2.8; 95%CI 1.3-6.0). Higher vaccination rates were also observed in Brussels-Capital Region among children who attended a daycare centre (OR 2.1; 95%CI 1.0-4.5).<sup>24</sup>

## DISCUSSION

### Meningococcal vaccination

Meningococcal C vaccination is a fundamental measure to prevent invasive meningococcal disease (IMD) among children and adolescents.<sup>25</sup> According to our revision, in countries with an active universal meningococcal vaccination program like the Netherlands and Belgium, uptake among parents of European children is strongly related with higher education level and socioeconomic status of the parents.<sup>7,10-12,26</sup>

Probably, in these cases, parents have higher awareness regarding meningococcal vaccination.<sup>9</sup> In particular, parents in Belgium can choose to have their child immunized in Mother and Child health or well-baby clinics, which are public organizations, or by a practitioner. Administration is free of charge when performed at the clinics, while a fee must be paid if the vaccine is administered by a GP or a pediatrician.<sup>26</sup> For these reasons, appropriate counseling about vaccination strategies represents an essential determinant for parents of 18-24 month old children in Belgium.<sup>8</sup> Conversely, in Poland pneumococcal vaccine is not included in the national immunization program.<sup>26</sup>

Nevertheless, in addition to free-of-charge vaccines listed in the mandatory immunization schedule, self-paid vaccinations are also recommended for Polish children (pneumococcal, meningococcal, rotavirus, etc.).<sup>26</sup> Indeed, in this context, determinants of vaccination uptake/refusal were mainly socioeconomic (family income, cost of the vaccine).<sup>26</sup>

Moreover, older parent age and a small number of children in the family, predictors that are already known in the literature and may be associated with higher socioeconomic status, were related with higher vaccination coverage.<sup>26,27</sup>

Among adolescents, a British study demonstrated the benefit of a school-based vaccination program.<sup>7</sup> In particular, UK students demonstrated better meningococcal vaccination coverage and attitudes compared to Irish student (no school-based vaccination strategy was implemented in Ireland).<sup>7</sup>

### Pneumococcal vaccination

The value of pneumococcal conjugate vaccination in IPD prevention is recognized worldwide.<sup>19,20</sup> Nonetheless, in some Eu-

European countries this is a recommended self-paid vaccination for children.<sup>26</sup> Therefore, in Poland the principal determinants related with vaccination uptake were socioeconomic (family income, cost of vaccination, etc.), similarly to those observed for meningococcal vaccination in the same country.<sup>12</sup> Likewise in Belgium, where pneumococcal vaccination was fully offered only in mother and child clinics or in daycare centres, vaccination coverage was higher precisely in these contexts.<sup>24,26</sup> Moreover, like in Poland, having only one child was a socioeconomic determinant associated with vaccination adherence.<sup>12,24</sup>

Conversely, among healthy European adults PPSV23 vaccination uptake was related with a strong recommendation by their own general practitioner.<sup>22,23</sup> Furthermore, the perception of pneumococcal disease danger and the perception of vaccination efficacy and effectiveness were factors strongly linked with adequate counseling by health care professionals.<sup>22,23</sup>

## CONCLUSIONS

Our results show that communication and information about meningococcal and pneumococcal vaccination for newborns and children should be targeted towards specific groups of par-

ents (low income or cultural level, younger age, different ethnicity). Moreover, it is essential to organize universal free-of-charge vaccination strategies. For healthy adults, conversely, the health professional's counseling activities on PPSV23 and in future on PCV13 vaccinations should be targeted on pneumococcal disease danger and pneumococcal vaccination efficacy and effectiveness. A strong recommendation for pneumococcal vaccination from general practitioners and a free-of-charge vaccination plan would also be important strategies.

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