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## Rates of Vaccination against *Streptococcus Pneumoniae* in Cochlear Implant Patients

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Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
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**Background:** *Streptococcus pneumoniae* can cause life-threatening illness, with invasive pneumococcal diseases (IPD) like meningitis, sepsis, bacteremic pneumonia, and bacteremia being major causes of morbidity and mortality. Studies have shown that patients who have had a cochlear implant, particularly children, have an increased risk of bacterial (pneumococcal) meningitis. Vaccination in patients with cochlear implants is important and recommended universally. The World Health Organization recommends the use of pneumococcal conjugate vaccines in all countries and considers their use to be a priority in all national immunization programs. The objective of this study was to assess rates of vaccination against *Streptococcus pneumoniae* in patients with cochlear implants who were implanted at the Institute of Physiology and Pathology of Hearing, Poland.

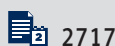
**Material/Methods:** We analyzed data from questionnaires administered to 2,628 patients who visited the Implants and Auditory Perception Department (IAPD) of the Institute of Physiology and Pathology of Hearing between January 2014 and March 2016.

**Results:** The percentage of vaccinated patients in the study group was 28.2%, most of whom (90.7%) were children. Among the children, 49.3% were vaccinated against *S. pneumoniae*, but the corresponding rate for adults was only 5.5%.

**Conclusions:** The percentage of patients with cochlear implants who received vaccination against *S. pneumoniae* was low, both in children and adults, but especially in adults comparing to available reports.

**MeSH Keywords:** Cochlear Implants • Streptococcus Pneumoniae • Vaccination

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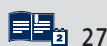
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## Background

*Streptococcus Pneumoniae* is a common commensal organism of the upper respiratory tract in children and adults. However it can also cause life-threatening illness, with invasive pneumococcal diseases (IPD) like meningitis, sepsis, bacteremic pneumonia, and bacteremia being major causes of morbidity and mortality [1]. Non-invasive pneumococcal diseases include otitis media, pneumonia, sinusitis, and less often osteitis, soft tissue infection, and endocarditis.

Disease caused by *S. pneumoniae* is recognized by the World Health Organization (WHO) as a major public health problem worldwide, with an estimated 1.6 million people dying of pneumococcal disease every year [2]. In the developed world, the major burden of disease is carried by children aged <2 years old and elderly people [2]. Among European countries, the reported burden of IPD varies [1]. In Poland, epidemiological data for 2010–2014 shows that people over 25 years of age account for the majority (79.7%) of cases of meningitis and encephalitis caused by *S. pneumoniae*; of those, persons 45–64 years old account for 51.6% of cases. However, the highest rate of incidence occurs in the 0–4 years age group (1.07 per 100,000 population) [3].

Beside older age or younger age, risk factors for IPD include ethnicity, geographic location, concomitant chronic illness, and attendance at day care centers [2,4]. In addition, studies have shown that patients who have had a cochlear implant, particularly children, have an increased risk of bacterial (pneumococcal) meningitis [5,6]. Cochlear implant is a neural prosthesis that uses electric stimulation to enhance or restore hearing in individuals with deafness. The function of a cochlear implant is to bypass the hair cells via direct electrical stimulation of surviving neurons in the auditory nerve. The prosthesis consists of two essential parts: the head-level unit that is worn behind the ear and the receiver/stimulator package which is implanted in a portion of the skull with an array of active electrodes inserted into the scala tympani through the round window membrane or through a larger drilled opening at or near the round window [7].

The Food and Drug Administration (FDA) reported that there were a total of 118 cases of meningitis related to cochlear implantation reported globally as of October 2003. In 67% of the meningitis cases with confirmed etiology, *S. pneumoniae* was the agent; these cases were all attributed to a cochlear implant with associated positioner [8]. However, even among children who received an implant without a positioner, the incidence of *S. pneumoniae* meningitis was higher than the same age group in the general population [5]. However, based on current knowledge, the exact route by which the bacterium reaches the meninges in the presence of a cochlear implant is

still unclear [9]. It is possible that a foreign body in the inner ear reduces the ability of immune cells to eliminate *S. pneumoniae*, although the molecular mechanism by which a foreign body impairs immune cell function is still unknown [10]. Other reported risk factors that have been found to be associated with post-implant meningitis include inner-ear malformations and cerebrospinal fluid (CSF) leakage [5,11].

Since IPD (including meningitis) is a vaccine-preventable illness [2,12,13], vaccination against *S. pneumoniae* in patients with cochlear implants is important and recommended universally [13,14]. WHO recommends the use of pneumococcal conjugate vaccines in all countries and considers their use to be a priority in all national immunization programs [2].

Currently, there are two types of pneumococcal vaccines on the market: a 23-valent polysaccharide vaccine (PPV23) and three conjugate vaccines: 7-valent (PCV7), 10-valent (PCV10), and 13-valent (PCV13) [2]. However, the availability of vaccines, and national immunization programs or vaccination strategies, varies between European countries [14].

In Poland, implementation of immunization programs and an individual's qualification for inoculation are regulated by the Act of December 5, 2008 on the Prevention and Control of Infections and Infectious Diseases in Humans. The Chief Sanitary Inspector releases a yearly bulletin containing a Program of Preventive Immunizations, which includes indicative criteria for vaccinations (obligatory or recommended) and their schedules.

Since 2009, vaccination against *S. pneumoniae* (PCV) has been mandatory in Poland for babies aged two months to five years of age who are in a high-risk group that has specific medical indications, while it is recommended for people over 65 years of age and for all at-risk groups regardless of age. Among other risk factors, a new factor, listed for the first time, is cochlear implant use [15]. Before 2009, *S. pneumoniae* vaccination was on the list of recommended vaccinations: it was first mentioned in 2003, and conjugate vaccine was included in the Immunization Program in 2006 [16]. On the whole, mandatory vaccinations in Poland are financed from public funds. Recommended vaccinations are voluntary, and the patient bears the cost of the vaccine.

The Cochlear Implant Program was established in Poland by Skarżyński in 1992 [17]. Since 2002, an electrode insertion in patients (both children and adults) with partial deafness is performed using an approach to the scala tympani directly through the round-window membrane in order to avoid loss of low-frequency hearing [18–21]. As of February 2016, more than 4,500 patients have been implanted at the Institute of Physiology and Pathology of Hearing (IPPH), constituting about 70% of cochlear

implants patients in Poland [22,23]. All patients and parents/caregivers of children who qualified for cochlear implant surgery are counselled regarding the potential risk of meningitis and the importance of appropriate vaccination against *S. pneumoniae*. However, the Institute does not administer the vaccine or maintain immunization records, a responsibility which falls to primary care providers. For this reason, all implant candidates are provided with a letter to their general practitioner regarding medical tests and procedures (including vaccination against *S. pneumoniae*) required for the surgery. However, vaccination is not a precondition for surgery, meaning the patient is not disqualified from surgery due to non-vaccination.

There are a very limited number of papers reporting on vaccination against *S. pneumoniae* coverage in cochlear implant patients. Data from USA cochlear implant centers show that vaccination rates range from 49% to 99% [24,25].

The aim of the study was to assess rates of vaccination against *S. pneumoniae* in patients implanted at the Institute of Physiology and Pathology of Hearing, Poland.

## Material and Methods

An interview questionnaire was used to assess vaccination against *S. pneumoniae* in patients implanted in the Institute of Physiology and Pathology of Hearing. The questionnaire was prepared as two versions: one for children and adolescents (patients <18 years old at the day of testing) and one for adults (patients ≥18 years old). The interview was conducted in the consulting room on the day of the visit by the doctor or nurse in charge of the patient. The questions were administered verbally to the patient or parents/caregivers. Before commencing, the interviewer informed the respondent (patient or parents/caretakers) about the objectives of the study, and all participants included in the study gave signed consent. The answers were first recorded on paper and then entered into a computer.

The questionnaire comprised two parts: part I contained vaccination-relevant questions, and part II contained questions relating to demography and social aspects of the respondent (age, education, employment, cochlear implant (CI) CI surgery date, province). Polish provinces were coded according to the ISO 3166-2 standard, which currently defines 16 provinces for the country. Territorial units were recorded according to the EU classification [26]. The accuracy of vaccination information for children (date of vaccination, vaccine type(s), number of doses) was verified with their Personal Child Health Record (PCHR); in adults the accuracy was verified with documents provided by the vaccination centers. Risk factors for IPD were confirmed with patient's medical records.

To assess the pneumococcal vaccination rates in patients with cochlear implant(s), questionnaire data from 2,628 patients who visited the Implants and Auditory Perception Department (IAPD) of the Institute of Physiology and Pathology of Hearing in 2014 or 2015 was analyzed. This group constituted 76.4% of all 3,438 patients who visited IAPD, at least once, between January 2014 and March 2016. The other 810 people visited IAPD on a day when none of the persons able to conduct the interview were present.

The study was approved by the Ethical Committee of the Institute of Physiology and Pathology of Hearing and conforms to the stipulations of the Declaration of Helsinki.

All statistical analyses were performed using Statistica 12.0 software with level of significance  $\alpha=0.05$ . Categorical variables were presented as percentages and tested with a Chi-square test ( $\chi^2$ ); continuous variables were reported as medians with range. Normal distribution was verified using a Kolmogorov-Smirnov test.

Written consent was obtained for all participants in the study. All procedures performed in the study were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

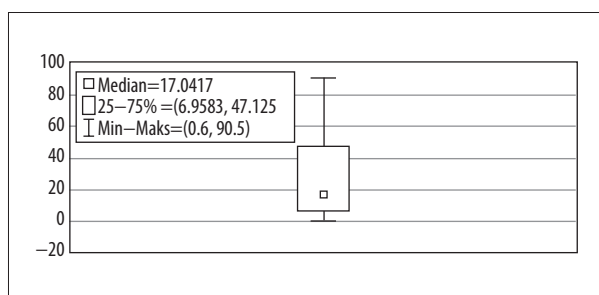
## Results

Characteristics of the study group are presented in Table 1. The study group constituted 60% of all the patients ( $n=4,352$ ) implanted at IPPH as of March 2016. Children and adolescents up to 18 years of age constituted 51.9% of both the study group and the population (Table 1). The youngest child was six months old, the oldest adult in the group was 90 years old (Figure 1). The proportion of females and males was 51.9% and 48.1% respectively, which was comparable with the sex distribution of the IPPH patients (51.7% and 48.3% females and males respectively). All 16 provinces from Poland were represented in the study population and the proportion of patients according to province of residence is presented in Figure 2. The majority of patients (78.7%) resided in cities (Table 1). Patients from each year of the CI Program were included in the study group (Figure 3).

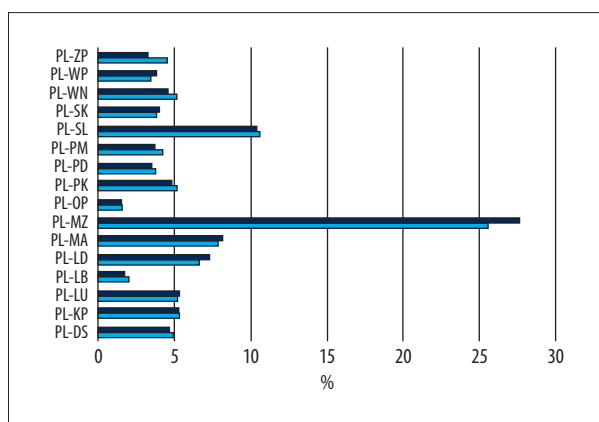
In total, 740 patients from the study group (28.2%) were vaccinated against *S. pneumoniae*. The majority (90.7%) of this group were children and adolescents up to 18 years of age. The rate in the pediatric population (49.2%) was significantly higher than in the adult population (5.5%) ( $\chi^2(1, n=2,628)=619.12, p<0.001$ ). The vaccination rate between the sexes was about the same for the whole group and within age groups ( $p>0.05$ ) (Table 2).

**Table 1.** Characteristics of the study group (n=2628) according to age, sex, and place of residence.

		Female		Male		Total
		n	%	n	%	
Children	Village	n	229	237	16.8	466
		%	49.1	50.9	18.7	100
	City	n	440	459	32.4	899
		%	48.9	51.1	36.2	100
Adults	Village	n	46	47	3.4	93
		%	49.5	50.5	3.7	100
	City	n	645	525	47.4	1170
		%	55.1	44.9	41.4	100
Total	n	1360	1268		2628	
	%		100		100	

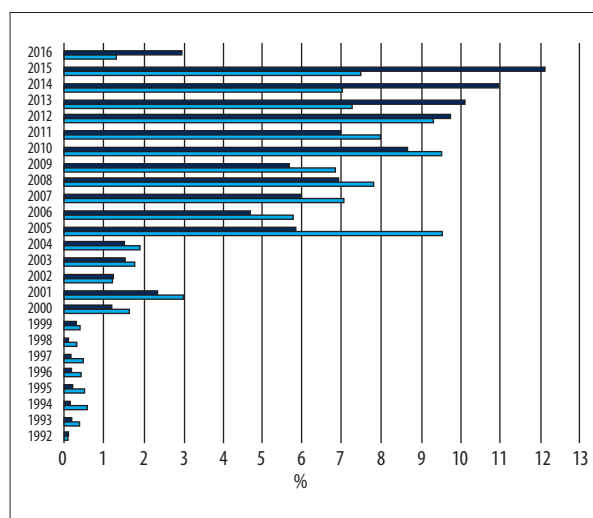


**Figure 1.** Age profile of patients in the study group.



**Figure 2.** Proportion of patients according to province of residence in the study group (light blue bars) and in the target population (dark blue bars).

Although 72.3% of vaccinated patients lived in cities, a significantly lower percentage of city dwellers were vaccinated (25.9%) compared to those living in villages (36.7%) ( $\chi^2(1, n=2,628)=25.44, p<0.0010$ ).



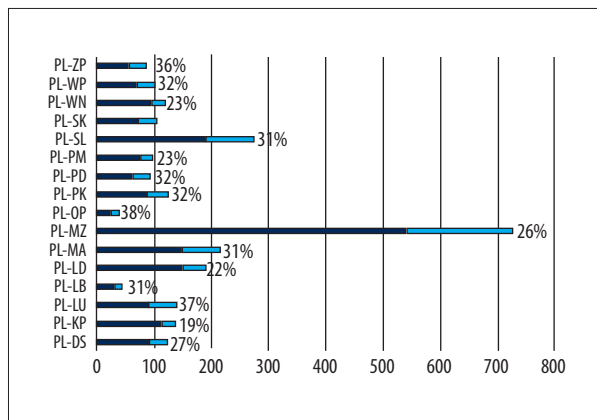
**Figure 3.** Percentage of patients implanted in consecutive years of the CI Program at the Institute of Physiology and Pathology of Hearing in the study group (light blue bars) and in the target population (dark blue bars).

Vaccination rates differed significantly according to province of residence ( $\chi^2(15, n=2,628)=28.67, p<0.05$ ), ranging from 19.4% in province PL-KP to 37.5% in province PL-OP (Figure 4). The highest absolute number of vaccinated CI patients (188; 7.6% of the vaccinated group) came from the Mazovian province (PL-MZ), which comprised 26% of all Mazovian CI patients. The highest rates of vaccinated patients in individual voivodeships were observed in Opole (PL-OP) with 37.5% and Lublin (PL-LU) with 36.9%.

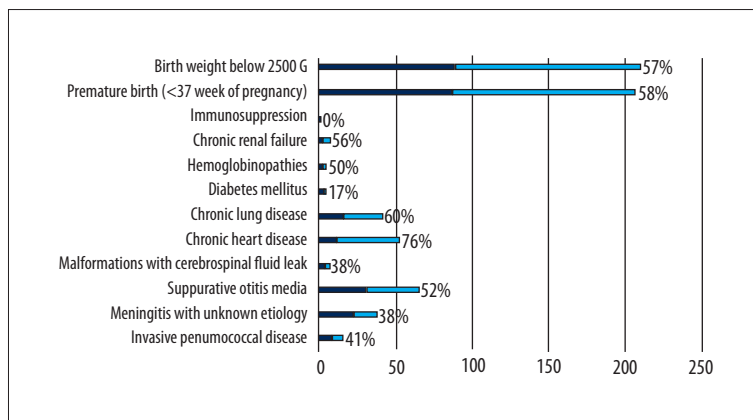
The vast majority of CI patients (98.4%) received primary vaccination against *S. pneumoniae* in the years 2006 to 2016. A similar percentage (98.1% or 726 out of 740) received primary

**Table 2.** Characteristics of the study group according to vaccination status.

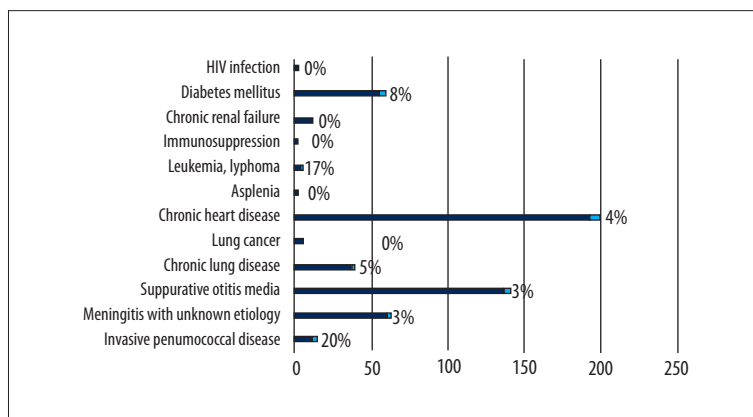
Streptococcus pneumoniae vaccination	All patients (n=2628)			Children (n=1365)			Adults (n=1263)		
	Female	Male	Total	Female	Male	Total	Female	Male	Total
Yes	375 (27.6%)	365 (28.8%)	740 (28.2%)	336 (50.2%)	335 (48.1%)	671 (49.2%)	39 (5.6%)	30 (5.2%)	69 (5.5%)
No	985 (72.4%)	903 (71.2%)	1888 (71.8%)	333 (49.8%)	361 (51.9%)	694 (50.8%)	652 (94.4%)	542 (94.8%)	1194 (94.5%)
Total	1360	1268	2628	669	696	1365	691	572	1263



**Figure 4.** Number of patients according to province of residence in the study group and the percentage of vaccinated (light blue) and non-vaccinated (dark blue) individuals.



**Figure 5.** Number of children with risk factors for IPD and the percentage of vaccinated (light blue) and non-vaccinated (dark blue) individuals according to risk factor.



**Figure 6.** Number of adults with risk factors for IPD and the percentage of vaccinated (light blue) and non-vaccinated (dark blue) individuals according to risk factor.



vaccination before CI surgery. There were 92.4% of children who were vaccinated with conjugate vaccine (PCV13, PCV10, or PCV7), and only 4.4% received a combination of both PCV7 or PCV10 or PCV13 and PPSV23. Only 1 child (2%) was vaccinated with polysaccharide PPSV23, and 7% of children who were vaccinated with PCV7 received an additional PCV13 vaccination. There were 382 patients in the study group (14.5%) who were implanted bilaterally; among this group 53.1% were vaccinated (97.5% of them were children).

The occurrence of at least one risk factor for IPD (other than CI implantation) was found in 843 CI patients (32.1% of the study group); 48.2% of them were children. In the pediatric population, at least one risk factor (other than CI implantation) was found in 29.7% of patients; in the adult group it was 34.6%. The most frequent risk factors reported among the pediatric population were premature birth and birth-weight below 2,500 g; in adults it was chronic heart disease (Figures 5, 6). Of premature and/or low birth-weight children, 55.6% received *S. pneumoniae* vaccination. Among children with two or more risk factors, 41.2% were not vaccinated against *S. pneumoniae*.

A history of meningitis and/or encephalitis caused by *S. pneumoniae* prior to hearing deterioration was confirmed in 32 cases (1.2% of the study group); only 10 patients from this group (31.3%) were vaccinated against *S. pneumoniae* before CI surgery. We identified no patients with post-implantation bacterial meningitis.

## Discussion

Data presented in our study confirm that a sizeable percentage of implanted patients (71.8%) have not been vaccinated against *S. pneumoniae*, even though it is suggested by government agencies, otolaryngological societies, implant manufacturers, and cochlear implantation centers [25]. The rate of vaccination in the study group is significantly lower compared to data from USA clinics [24,25]. Although no patients were identified with post-implantation bacterial meningitis in the group, there continued to be new cases of meningitis in the general population. In the last three years in Poland, about 3,000 cases per year of meningitis and/or encephalitis of bacterial, viral, and/or aseptic etiology have been recorded [3,27]. Almost 200 cases of meningitis and/or encephalitis arose in 2014 (an incidence rate of 0.51 per 100,000 population), a figure 3.7% greater than in 2013. These data confirms that efforts should be undertaken to increase the rate of vaccinated patients.

Aside from the National Immunization Program, immunization strategies in Poland involve financing from local or regional initiatives. Within the framework of healthcare programs implemented in Poland in 2014, 35 pneumococcal vaccination

programs were commenced and/or continued, involving 12 out of 16 voivodships. The largest number of programs was undertaken in the Mazovian voivodship (PL-MZ; six programs), followed by the Swietokrzyskie (PL-SK) and Lublin (PL-LU) voivodships (five each). Nearly 70% of the programs aimed at preventing pneumococcal infections were implemented by communes (LAU-2 territorial unit), 30% by city districts (LAU-1), and 10% by districts (LAU-1). Vaccination programs mostly included children up to five years old, with the largest group being children aged 24–36 months old. We observed that rates of vaccination against *S. pneumoniae* were related to province of residence and we speculate that the high percentage of vaccinated CI patients in Swietokrzyskie and Lublin is the result of actions taken by local governments to promote and finance vaccination. The low percentage of vaccinated patients from Mazovian province (25.8%) may reflect a high number of parents who objected to their children being vaccinated.

The cost of vaccination might be one factor that affects the percentage of vaccinated patients. However, in Poland since 2009 all children at risk up to five years of age (including those before or after CI surgery) are entitled to free vaccination against *S. pneumoniae*. This probably explains the high percentage of vaccinations (87.7%) performed in the group from 2009 to 2016. However, in this period, CI surgery was performed on 706 children aged five months to five years, and only 70.4% of babies from this group received vaccination.

Patients who at the time of CI surgery were particularly vulnerable to IPD, i.e., children implanted before two years of age and the group of adults aged 65+, comprised 23.7% and 7.3% of the study group, respectively; 66.3% of children and 9.4% of adults from these groups were vaccinated against *S. pneumoniae*. All CI patients and parents confirmed that they had heard about vaccination against *S. pneumoniae*; however, most of those unvaccinated had not received consistent information from local health providers, or they understood that vaccination was recommended and optional, meaning not necessary.

To increase the percentage of cochlear implant patients vaccinated against *S. pneumoniae*, the introduction of mandatory vaccination against invasive pneumococcal disease for all children has been proposed in Poland, and some work has already been undertaken in this direction. One can assume that if local programs continue, and there is a total or partial exemption from costs associated with vaccination, more parents will decide to immunize their children.

To increase awareness of the threat of invasive pneumococcal disease, healthcare providers should review the vaccination records of their patients who are either CI recipients or candidates for CIs to ensure they have received pneumococcal vaccinations based on age-appropriate schedules for persons at high risk [2].

## Conclusions

The percentage of patients with cochlear implants who received vaccination against *S. pneumoniae* assessed by means

of questionnaire was very low, both in children but especially in adults. Systematic approaches, including dissemination of information and effective epidemiological surveillance, are needed to increase vaccination rates in CI users.

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