

Prevalence of High-Risk Underlying Conditions for Pneumococcal Disease Among People Over 50 Years in Catalonia, Spain

Angel Vila-Corcoles^{1,2*}, Imma Hospital¹, Olga Ochoa-Gondar^{1,2}, Cinta de Diego¹, Eva Satue¹, Maria Aragon³

¹Primary Health Care Service "Camp de Tarragona", Institut Catala de la Salut, Tarragona, Spain

²Primary Care Research Institute (IDIAP Jordi Gol), Barcelona, Spain

³Information System for the Improvement of Research in Primary Care (SIDIAPI), Primary Care Research Institute Jordi Gol, Universitat Autònoma de Barcelona, Barcelona, Spain

Abstract

Background: Published data on the frequency and distribution of high-risk factors for pneumococcal disease are limited. This study investigated the prevalence of high-risk underlying conditions for pneumococcal disease among people over 50 years in Catalonia, Spain.

Methods: Cross-sectional population-based study including 2,033,465 individuals aged 50 years or older registered on 01/01/2015 in the Catalan Health Institute. A previously validated institutional research clinical Database was used to identify high-risk conditions to suffer pneumococcal disease (functional or anatomic asplenia, cochlear implants, cerebrospinal fluid [CSF] leaks and/or immunocompromising conditions). Prevalence of risk conditions was compared according to gender and age strata.

Results: Of the total 2,033,465 study population, an amount of 176,600 persons (8.7%) had any high-risk condition. Prevalence of high-risk subjects did not substantially differ by gender (9.2% in men vs. 8.2% in women; $p < 0.001$), but considerably increased with increasing age (5.1% in 50-64 years vs. 10.6% in 65-79 years vs. 16.1% in people 80 years or older; $p < 0.001$).

Overall, 294 individuals (<0.1%) had anatomical or functional asplenia, 76 (<0.1%) cochlear implants, 41 (<0.1%) CSF leaks, 3,854 (0.2%) had immunodeficiency/AIDS, 16,815 (0.8%) had severe renal disease (nephrotic syndrome or renal failure), 5,034 (0.2%) had received bone marrow transplantation, 103,948 (5.1%) had recent cancer (diagnosed within 5 prior years) and 72,040 (3.5%) received immunosuppressive medication/radiotherapy.

Conclusion: In our setting, almost ten percent of people over 50 years have any high-risk factor for pneumococcal vaccination, basically immunocompromising conditions.

Keywords: *Streptococcus pneumoniae*; Risk factors; Underlying conditions; Pneumococcal disease; Pneumococcal vaccines

Introduction

Infections due to *Streptococcus pneumoniae* are a major cause of morbidity and mortality worldwide. According to the World Health Organization, pneumococcal disease causes an estimated 1.6 million deaths annually among all-age populations throughout the world [1]. To date, after the introduction of routine childhood immunization, high-risk individuals and older adults suffer the greatest burden of pneumococcal disease in developed countries. At present, two anti-pneumococcal vaccines are available for use in adults: the "classical" 23-valent pneumococcal polysaccharide vaccine (PPV23) and the "new" 13-valent protein-polysaccharide conjugate vaccine (PCV13).

Among adult populations, apart from the presence of low socioeconomic status or high-risk behaviours (e.g. smoking and/or alcohol abuse), it is known that the risk of developing invasive pneumococcal disease (IPD) is greatest in persons with certain high-risk underlying medical conditions, such as anatomic or functional asplenia, cochlear implants, cerebrospinal fluids (CSF) leaks, immunodeficiency's and immunocompromising conditions [2-4].

Although some studies have reported major comorbidities and underlying conditions among hospitalised patients with IPD, population-based data on the prevalence of these high-risk conditions is limited. Indeed, despite these patients are considered a major target group for pneumococcal vaccination, data about its true prevalence in most settings is unknown [4-10].

The accurate knowledge of prevalence for distinct risk conditions is important to estimate the true magnitude of at-risk groups and

estimate the size of distinct target populations to implement different antipneumococcal vaccination strategies. In the present study, we investigated the prevalence of distinct high-risk medical conditions for pneumococcal disease among middle-aged and older adults in Catalonia, Spain.

Methods

This is a cross-sectional study involving 2,033,465 individuals aged 50 years or older, who were registered in any of the Primary Health Care Centres (PHCCs) of the Catalan Health Institute on January 1, 2015 (date of survey). The study was approved by the ethical committee of the institution (file P14/134) and was conducted in accordance with the general principles for observational studies.

In Catalonia, there are 358 PHCCs (comprised by family physicians, nurses, social workers and support staff) which are distributed by geographical area and are responsible for the health care of the population in their areas. The *Catalan Health Institute* manages 274

***Corresponding author:** Angel Vila Corcoles, Primary Health Care Service "Camp de Tarragona", Institut Catala de la Salut, Tarragona, Spain, E-mail: avila.tarte.ics@gencat.cat

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PHCCs (76.5%), serving a population of approximately five millions people; the remaining 84 PHCCs are managed by other providers. Doctors and nurses systematically use electronic medical records to record medical diagnoses, underlying conditions, prescriptions, and other clinical, patient management activities coded according to the International Classification of Diseases, 10th Revision (ICD-10).

The *Catalonian Health Institute Information System for the Development of Research in Primary Care* ("SIDIAP" database) compiles coded clinical information from the Electronic PHCC's records, and it has been used as main data source for this report. Quality criteria for clinical data and research utility of the SIDIAP database have been reported [11,12]. The SIDIAP sample is representative of the general Catalan population in terms of geography, age and gender distributions, according to the official census [11].

The "SIDIAP" research database was used to identify the following high-risk conditions in each study subject: functional or anatomic asplenia (ICD10 codes D57, D73 and Q89), cochlear implants (Z96.2 and Z45.3), CSF leaks (Z98.2), immunodeficiency/AIDS (D80-D84 and B20-B24), severe renal disease (including nephrotic syndrome [N04 and N39.1] and/or chronic renal failure with glomerular filtration ≤ 30 ml/min), bone marrow transplantation (Z94), solid organ or haematological neoplasia diagnosed within previous 5 years (C00-C97) and/or immunosuppressive medication/radiotherapy in prior 12 months (specific SIDIAP codes). We assumed that information in electronic clinical records was complete, so a condition was considered absent if it was not recorded.

The statistical differences between prevalence for distinct risk conditions according distinct population subgroups were evaluated using the Chi-squared tests or Fisher's test as appropriate, considering statistical significance at $p < 0.05$ (two-tailed). Data were analyzed using the SPSS 18 statistical package.

Results

Of the total 2,033,465 study population, mean age was 66.1 years old (SD: 11.5), being 935,705 (46%) men and 1,097,760 (54%) women. By age strata, 1,021,648 (50.2%) were 50-64 years old, 691,283 (34.0%) were 65-79 years old and 320,534 (15.8%) were aged 80 years or more.

Overall, 294 persons (<0.1%) had anatomical or functional asplenia, 76 (<0.1%) cochlear implants, 41 (<0.1%) CSF leaks, 3,854 (0.2%) immunodeficiency/AIDS, 16,815 (0.8%) had severe renal disease, 5,034 (0.2%) had received bone marrow transplantation, 103,948 (5.1%) had recent cancer and 72,040 (3.5%) received immunosuppressive medication/radiotherapy.

A total of 176,600 persons (8.7%) had any of the above mentioned risk condition and may be considered high-risk subjects for pneumococcal vaccination. Of them, 152,221 presented one high-risk condition, 23,301 presented two conditions and 1,078 presented three or more conditions.

Prevalence of high-risk subjects did not substantially differ by gender (9.2% in men vs. 8.2% in women; $p < 0.001$), but considerably increased with increasing age (5.1% in 50-64 years vs. 10.6% in 65-79 years vs. 16.1% in 80 years or older; $p < 0.001$). Prevalence for each one of the distinct high-risk conditions, according to gender and age strata, is shown in Tables 1 and 2, respectively.

Discussion

Published data about population-based prevalence of risk factors/underlying conditions to suffer pneumococcal diseases is limited [7,13,14]. The present study, which included more than 2 millions people 50 years or older in Catalonia (Spain), estimates the prevalence for most high-risk factors/conditions related to severe pneumococcal infections described in the literature [4,7,15].

Gender Risk condition	MEN N=935,705 n (%)	WOMEN N=1,097,760 n (%)	p	Total N=2,033,465 n (%)
Asplenia	141 (<0.1)	153 (<0.1)	0.504	294 (<0.1)
Cochlear Implant	27 (<0.1)	49 (<0.1)	0.067	76 (<0.1)
CSF Leaks ¹	17 (<0.1)	24 (<0.1)	0.559	41 (<0.1)
Immunodeficiency/AIDS	2,762 (0.3)	1,092 (0.1)	<0.001	3,854 (0.2)
Severe Renal Disease ²	6,931 (0.7)	9,884 (0.9)	<0.001	16,815 (0.8)
Bone Marrow Transplantation	3,096 (0.3)	1,938 (0.2)	<0.001	5,034 (0.2)
Recent Neoplasia ³	55,475 (5.9)	48,473 (4.4)	<0.001	103,948 (5.1)
Immunosuppressive Medication/Radiotherapy ⁴	29,408 (3.1)	42,632 (3.9)	<0.001	72,040 (3.5)

Table 1: Prevalence of distinct high risk conditions for pneumococcal disease, by gender among Catalonian people 50 years or older.

¹CSF: Cerebrospinal Fluid

²Severe renal disease includes nephrotic syndrome and/or chronic renal failure with glomerular filtration ≤ 30 ml/min

³Recent neoplasia includes solid organ or haematological neoplasia diagnosed within previous 5 years

⁴Immunosuppressive medication/radiotherapy administered in prior 12 months

Age group Risk condition	50-64 years N=1,021,648 n (%)	65-79 years N=691,283 n (%)	≥ 80 years N=320,534 n (%)	p
Asplenia	186 (<0.1)	83 (<0.1)	25 (<0.1)	<0.001
Cochlear Implant	23 (<0.1)	31 (<0.1)	22 (<0.1)	<0.001
CSF Leaks ¹	11 (<0.1)	16 (<0.1)	14 (<0.1)	<0.001
Immunodeficiency/AIDS	3,111 (0.3)	618 (0.1)	125 (0.0)	<0.001
Severe Renal Disease ²	1,605 (0.2)	4,783 (0.7)	10,427 (3.3)	<0.001
Bone Marrow Transplantation	2,415 (0.2)	2,251 (0.3)	368 (0.1)	<0.001
Recent Neoplasia ³	30,339 (3.0)	47,047 (6.8)	26,562 (8.3)	<0.001
Immunosuppressive Medication/Radiotherapy ⁴	22,319 (2.2)	28,902 (4.2)	20,819 (6.5)	<0.001

Table 2: Prevalence of distinct high risk conditions for pneumococcal disease, according to age strata in study population.

¹CSF: Cerebrospinal Fluid

²Severe renal disease includes nephrotic syndrome and/or chronic renal failure with glomerular filtration ≤ 30 ml/min

³Recent neoplasia includes solid organ or haematological neoplasia diagnosed within previous 5 years

⁴Immunosuppressive medication/radiotherapy administered in prior 12 months

According our results, almost ten percent (8.7%) of the general population over 50 years in our setting have any high-risk condition to suffer pneumococcal disease. This proportion is too similar in men (9.2%) and women (8.2), but it is considerably higher in older than in younger subjects (5.1% in 50-64 years vs. 16.1% in 80 years or older).

Our results may have implications for policy makers, having special interest to know the true magnitude of certain target population subgroups and evaluate possible cost-effectiveness of different prevention strategies. To date, there are not universal consensus for pneumococcal vaccination schedules in adults [1,9,10,16,17].

At present, experts are evaluating different alternative vaccination strategies for adults (basically, maintaining "classical" PPV23 recommendations for adults, changing PPV23 for "new" PCV13 recommendation in some risk groups, or adding PCV13 recommendation for all or some target adult population subgroups). Nevertheless, a direct comparison between clinical effectiveness of PPV23 vs. PCV13 in adults, together a better knowledge of the magnitude of possible indirect effects from PCV13 childhood vaccination in adults, is necessary before a well informed decision can be made [18]. Apart from its possible better efficacy than PPV23, the lower serotype coverage of the PCV13 is a shortcoming for routine use of PCV13 alone in adult populations. A sequential strategy using both PCV13 and PPV23 vaccines could be a way to achieve greater effectiveness among high-risk subjects. In this way, according to current recommendations of the Advisory Committee on Immunization Practices (ACIP) of the Center for Diseases Control and Prevention, a sequential dual pneumococcal vaccination (PCV13 plus PPV23) is recommended for persons aged 65 years or older (with or without underlying conditions) and persons 19-64 years with CSF leaks, cochlear implants, functional or anatomic asplenia, sickle cell disease or other hemoglobinopathy, congenital or acquired asplenia, immunocompromised persons (congenital or acquired immunodeficiency, human immunodeficiency virus infection, chronic renal failure, nephrotic syndrome, leukemia, lymphoma, Hodgkin disease, generalized malignancy, iatrogenic immunosuppression [treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy], solid organ transplant and multiple myeloma) [10,16]. At present, ACIP recommends pneumococcal vaccination using exclusively PPV23 for immunocompetent persons 19-64 years with other comorbidities or risk conditions such as pulmonary or cardiac disease, diabetes mellitus, alcoholism and smoking) [9].

Our study has several strengths. Study design was population-based and large enough to assess accuracy prevalence of main high-risk conditions related to invasive pneumococcal infections. As limitation, although the validity of clinical data source was previously checked, information bias may have occurred if some comorbidity/underlying condition was not recorded, but such misclassification would likely be small considering that the prevalence observed for most risk conditions fit with data previously reported in the literature [7,12,15]. In North Europe, a population-based study including 5.2 million Finnish all-age people, approximately four percent of the population had any high-risk condition for pneumococcal disease (organ or bone marrow transplantation, chronic renal failure, cancer diagnosed within previous 5 years, immunodeficiency or HIV infection) [19]. The impact of possible information bias may be higher in relation to diseases such as AIDS (stigma and legal problems if the patient does not authorize registration) or diseases that are managed in the hospital setting (especially if survival after diagnosis was short).

We have not available data about the prevalence of some high-risk conditions (e.g. solid organ transplantations); so, the global burden of high-risk group for pneumococcal infections may have been slightly underestimated. In addition, the global magnitude of certain high-risk conditions may also have been underestimated in some cases considering that the study population did not include persons less than 50 years of age.

Conclusion

Our data shows that a considerable proportion (almost ten percent) of overall people 50 years or older in our setting have any high-risk condition (especially immunocompromising conditions) to suffer invasive pneumococcal disease and, consequently, they should be considered serious candidates for pneumococcal vaccination. We emphasize that it is important to estimate accurately the prevalence of high-risk individuals because these persons are at the center of the current debate on whether or not to extend the possible vaccination programs (PPV23, PCV13 or PPV23+PCV13) for all or only certain high-risk individuals.

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Contributors

A. Vila-Corcoles and O. Ochoa-Gondar designed the study, assessed outcomes, wrote and edited the paper; M. Aragon obtained the data; O. Ochoa-Gondar did statistical analyses.

The following persons are members of the EPIVAC study group: A. Vila-Corcoles, O. Ochoa-Gondar, I. Hospital, C. de Diego, E. Satue, E. Salsench, J. Blade, X. Ansa, JA. Guzman, F. Gomez, X. Raga, MO. Perez, F. Ballester, R. Magarolas, L. Esteban, E. Figuerola and F. Ramos.

A. Vila-Corcoles, I. Hospital, O. Ochoa-Gondar, C. de Diego and E. Satue designed the study, assessed outcomes wrote and edited the paper; M. Aragon obtained the data; I. Hospital did statistical analyses; the two first listed authors contributed similarly to this work.

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