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Hospital burden of pneumococcal disease in Spain (2016–2022): A retrospective study

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ABSTRACT

Pneumococcal disease is a leading cause of morbidity and mortality worldwide. From 2016 to 2022, 358,603 hospitalized patients were identified as having pneumococcal disease. The overall annual hospitalization rate was 108.9 hospitalizations per 100,000 people, which significantly increased with age, reaching 748.0 hospitalizations per 100,000 among those aged ≥90 years. The hospitalization rates for pneumococcal pneumonia, meningitis, and sepsis were 25.4, 0.7, and 3.5 hospitalizations per 100,000 people, respectively, reaching the highest rates in those ≥90 years of age for pneumococcal pneumonia and sepsis, with 241.6 and 22.0 hospitalizations per 100,000 people, respectively, and in those <1 year of age for meningitis, with 3.4 hospitalizations per 100,000 people. The total number of deaths among all hospitalized pneumococcal infection patients was 51,668, with a total case fatality rate of 14.4%. The case fatality rates for pneumococcal pneumonia, meningitis, and sepsis were 7.9%, 10.6%, and 19.8%, respectively. The case fatality rate increased dramatically with age. Most patients presented with at least one underlying condition. The case fatality rate among patients with at least one comorbidity was significantly higher ($p < .05$) than that among patients without underlying conditions (16.0% vs. 3.2%, respectively), with a fivefold greater probability of death (OR = 5.7). During this period, the annual cost of hospitalizations for the health system exceeded EUR 383 million. Thus, the use of new broad-spectrum PCVs and improved vaccination protocols for elderly individuals and people with comorbidities could help reduce the high hospital burden of disease and mortality due to pneumococcal infection in our country.

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Introduction

Pneumococcal disease caused by *Streptococcus pneumoniae* (*S. pneumoniae*) is a leading cause of morbidity and mortality worldwide, particularly in children and elderly individuals.[1] It is the primary cause of acute respiratory and invasive infections[2], leading to a high number of hospitalizations and high costs.[2] Pneumococcal disease causes a variety of clinical syndromes, the most important of which are pneumococcal pneumonia, the most common clinical presentation, meningitis, and sepsis.

According to the Global Burden of Disease Study 2021, *S. pneumoniae* is responsible for an estimated 97.9 million cases and 505,000 deaths globally.[2] In Spain, the annual hospitalization rate due to pneumococcal disease (2016–2020) was 108.4/100,000 in the population, reaching 657.5/100,000 in those aged ≥85 years.[3] Age is the most critical risk factor as it increases the morbidity and mortality of pneumonia. Additionally, comorbidities, which are more common in older age groups, increase morbidity and mortality.[2,4,5] Several factors contribute to the continuing impact of pneumonia on health systems, including challenges in microbiological diagnoses, antibiotic resistance, and changes in epidemiology since the introduction of vaccination.[1]

From a preventive point of view, the best strategies include improving vaccine coverage and vaccination programs in children and elderly individuals and reducing preventable comorbid conditions in the elderly.[6,7] The 23-valent polysaccharide vaccine (PPV23) and pneumococcal conjugate vaccine (PCV) 13 (PCV13) are the most widely used vaccines globally[7,8]. Four vaccines have been commercialized in Spain: PPV23, PCV10, PCV13, and PCV20.[3] PPV23 was funded by the Spanish public health care system in 2000. PCV13 (serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9 V, 14, 18C, 19F, 19A, and 23F included) was authorized in 2010 for the private market[9] and was expanded to be publicly funded by National Immunization Programs in 2015–2016. The Spanish vaccination policy recommends PCV13 for children following a 2 + 1 schedule.[6,10] PCV13 has proven to be a very useful preventive measure in children and has indirectly led to fewer cases of pneumococcal disease caused by vaccine-preventable serotypes in adults, demonstrating important herd protection for Spanish adults.[6,9,11] For adults, recommendations are heterogeneous throughout the country. The Ministry of Health recommends routine vaccination with PPV23 for all immunocompetent adults aged ≥65 years and

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a sequential vaccination schedule for high-risk adults (PCV13+PPV23).[6,10,12] However, an increase in cases caused by some PPV23 serotypes was observed. With low coverage, the global impact on the adult population's disease burden is limited[7]. Thus, communities included PCV13 for immunocompetent adults.[6,12] In addition, since PCV20 was approved in 2022, all communities have incorporated it into their vaccination schedules for the elderly and high risk groups ≥18 years old. In addition, some communities also use PCV20 for immunosuppressed populations ≥18 years old and/or as a special guideline in individuals after hematopoietic precursor transplantation.

This retrospective study aimed to provide population-based estimates of the burden of hospitalization for pneumococcal disease, specifically for pneumococcal pneumonia, pneumococcal sepsis, and pneumococcal meningitis, in the general population in Spain over seven years (2016–2022). We also aimed to identify national-level risk factors to guide recommendations for pneumococcal vaccination in the population.

Materials and methods

This retrospective study used the Spanish National Hospital Data Information System (Conjunto Mínimo Básico de Datos; CMBD) maintained by the Ministry of Health[13]. This system covers an estimated 98% of public hospitals and provides a comprehensive hospitalization registry. The Spanish Ministry of Health has validated the CMBD for data quality and overall methodology. It is a valuable system for epidemiological analysis[13], and since 2016 uses the 10th Clinical Revision of the International Classification of Diseases (ICD-10-CM).[14] Compulsory health insurance covers an estimated 99.5% of the Spanish population, and even persons not covered by it can be treated in the hospitals of the health care system.

The Rey Juan Carlos University Ethics Committee determined that ethical approval for this study was not required. All retrospective cases diagnosed with pneumococcal disease, according to the ICD-10-CM[14] (With an algorithm including any pneumococcal infection- *Streptococcus pneumoniae as the cause of diseases classified elsewhere-)* between January 2016 and December 2022, were collected. Analysis was broken down for pneumococcal pneumonia, pneumococcal sepsis and pneumococcal meningitis (*J13-pneumonia due to Streptococcus pneumoniae, 40.3-sepsis due to Streptococcus pneumoniae, G 00.1-pneumococcal meningitis*. All age groups were studied, with particular emphasis on those under 2 years of age and those over 65, both overall and by risk group. The necessary codes related to the risk factors for interest were also considered.

Comorbidities were also considered risk factors for pneumococcal disease. Thus, ORs by risk factor were calculated for patients with pneumococcal disease exposed to the following risk factors: HIV, solid tumors, hematological malignancies, immunodeficiencies, diabetes, arterial hypertension (AHT), cardiopulmonary disease, chronic lower respiratory tract disease, cerebrovascular disease, chronic obstructive pulmonary disease (COPD), asthma, acute renal failure, and liver disease.

Statistical analysis

The data on the population covered by the hospitals used in this study were obtained from the CMBD adjusted for population figures from municipal registers. It was assumed that the distribution by age of the population covered by these public hospitals was equal to that of the general population. Patient data were anonymized and deidentified prior to analysis.

We calculated the average number of hospitalizations per year, the annual incidence of hospital admissions (per 100,000 population), and the mortality rate (per 100,000 population). The average length of hospital stay (ALOS) was calculated as the total length of stay divided by the total number of hospitalizations. The case fatality rate (%), which reflects the severity of cases, was calculated by dividing the number of deaths by the total number of hospitalizations. The Ministry of Health estimated the cost of hospitalizations to healthcare system data. The cost was calculated by considering the diagnosis cost group, the total cost, and the number of discharges. The diagnostic cost group was based on diagnosis-related groups (DRGs) for hospitalized patients based on the International Classification of Disease (ICD) classification, age, sex, and resource consumption. Each group has a similar weight in hospital costs and can be applied to each related patient. DRG calculations were performed by 3 M's with Core Grouping System software.

The chi-square test with confidence intervals (95% CIs) was used to evaluate significant differences in proportions. Logistic regression was used to assess the differences in case fatality rates. Poisson regression models were used to measure the differences in hospitalization, mortality, and case fatality rates during the study period by age group and sex.

For all tests, the significance level was set at $p < .05$. Statistical analyses were performed via SPSS 27 and Stata 16.1 software.

Results

Hospitalizations

From 2016 to 2022, 358,603 hospitalized patients in Spain were identified as having pneumococcal disease. Of these, 57.4% (205,806) were male, and 42.6% (152,797) were female. Among the age groups, 1.9% were <2 years, 64.2% were ≥65 years, and 33.9% were 2–64 years old. The average length of stay was 8 days (IQR: 6,0), with a mean cost of 7,490.7€ [SD: 10388.14€) per hospitalization. The annual cost of hospitalizations for the health system was more than EUR 383 million.

The overall annual hospitalization rate was 108.9 hospitalizations per 100,000 people (95% CI: 108.6–109.3) and 127.6 (95% CI: 127–128.1) for men (Table 1). The only age range in which no significant differences were observed in terms of sex was between 1 and 14 years. However, significant differences ($p < .05$) were found between the age groups. Hospitalization rates were highest in the population <1 year of age (185.4; CI 95%: 180.1–190.7). Rates then decreased and increased again from the age of 55–59 years (107.85; CI 95%: 106.4–109.1) until reaching the highest incidence in patients aged 85–89 years (615.5; CI 95%: 609.5–621.4) and older than 90 years (748.0; CI 95%: 739.3–756.8) (Table 1). Significant differences

Table 1. Hospitalization rate by sex and age group related to pneumococcal disease, pneumococcal pneumonia, meningitis, and sepsis in Spain (2016–2022).

		Hospitalization Rate/per 100,000 (CI 95%)			
Sex	Age group	Pneumococcal disease	Pneumococcal Pneumonia	Pneumococcal Meningitis	Pneumococcal Sepsis
Male	Total	127.6 (127–128.1)	29.5 (29.2–29.7)	0.8 (0.7–0.8)	4.4 (4.3–4.5)
	<1 year	200.9 (193.2–208.6)*	9.4 (7.8–11.1)*	4.1 (3–5.2)	4.4 (3.3–5.6)
	1.00 years	79.7 (75.0–84.4)	15.5 (13.4–17.5)	1.7 (1.0–2.4)	2.9 (2.0–3.7)
	2.00 years	56.5 (52.6–60.3)	11.8 (10–13.5)	1.2 (0.6–1.7)	2.0 (1.3–2.7)
	3.00 years	47.4 (43.9–50.8)	12.2 (10.4–13.9)	0.9 (0.4–1.4)	0.6 (0.2–1.0)
	4.00 years	34.9 (31.9–37.8)	8.3 (6.9–9.7)	0.9 (0.4–1.4)	0.8 (0.4–1.3)
	5–9 years	17.7 (16.8–18.6)	3.0 (2.7–3.4)	0.3 (0.2–0.4)	0.3 (0.2–0.4)
	10–14 years	11.2 (10.5–11.9)	1.3 (1.0–1.5)	0.3 (0.2–0.4)	0.3 (0.2–0.4)
	15–19 years	16.2 (15.3–17.0)*	2.7 (2.3–3.0)*	0.1 (0.0–0.2)	0.4 (0.3–0.6)
	20–24 years	15 (14.2–15.8)*	2.7 (2.3–3)	0.1 (0.0–0.1)	0.4 (0.3–0.5)*
	25–29 years	16.7 (15.8–17.5)*	3.7 (3.3–4.1)*	0.2 (0.1–0.3)	0.7 (0.5–0.9)*
	30–34 years	22.1 (21.2–23.0)*	5.5 (5.1–6)*	0.3 (0.2–0.4)	1.0 (0.8–1.2)*
	35–59 years	28.5 (27.6–29.5)*	7.7 (7.2–8.2)*	0.5 (0.3–0.6)*	1.3 (1.1–1.5)*
	40–44 years	39.0 (38.0–40.1)*	10.8 (10.3–11.4)*	0.6 (0.5–0.8)*	1.8 (1.6–2.0)*
	45–49 years	56.3 (55.1–57.6)*	14.0 (13.3–14.6)*	0.6 (0.4–0.8)	2.8 (2.5–3.1)*
	50–54 years	88.0 (86.4–89.7)*	19.2 (18.5–20.0)*	0.8 (0.6–1.0)	3.4 (3.1–3.7)*
	55–59 years	130.9 (128.8–133)*	26.1 (25.1–27.0)*	1.0 (0.8–1.1)	5.1 (4.7–5.5)*
	60–64 years	195.7 (192.9–198.5)*	36.9 (35.7–38.1)*	1.3 (1.1–1.6)	7.2 (6.7–7.7)*
	65–69 years	275.2 (271.5–278.8)*	54.7 (53.1–56.3)*	1.8 (1.5–2.1)	9.6 (8.9–10.3)*
	70–74 years	368.6 (364.1–373.1)*	81.9 (79.8–84.0)*	1.7 (1.4–2.0)	12.0 (11.2–12.9)*
	75–79 years	492.7 (486.6–498.8)*	113.9 (111.0–116.8)*	1.7 (1.3–2)	17.2 (16.0–18.3)*
	80–84 years	648.3 (640.3–656.4)*	19.4 (18.0–20.8)*	1.3 (1.0–1.7)	19.4 (18.0–20.8)*
	85–89 years	862.6 (850.9–874.2)*	246.0 (239.7–252.2)*	0.9 (0.5–1.2)	26.9 (24.9–29.0)*
	≥90 years	1075.7 (1056.2–1095.1)*	351.7 (340.6–362.9)*	0.6 (0.1–1.1)	32.0 (28.6–35.3)*
Female	Total	91.0 (90.6–91.5)	21.5 (21.3–21.7)	0.7 (0.6–0.7)	2.6 (2.5–2.7)
	<1 year	169.0 (161.8–176.3)	6.8 (5.3–8.2)	2.7 (1.8–3.6)	3.6 (2.5–4.7)
	1.00 years	78.0 (73.3–82.8)	13.8 (11.8–15.8)	1.1 (0.5–1.6)	3.4 (2.4–4.4)
	2.00 years	56.2 (52.2–60.1)	12.5 (10.6–14.4)	1.2 (0.6–1.7)	1.2 (0.6–1.7)
	3.00 years	48.6 (45.0–52.2)	13.2 (11.3–15.0)	0.7 (0.3–1.1)	0.6 (0.2–1.0)
	4.00 years	39.1 (36.0–42.3)	8.5 (7.0–9.9)	0.6 (0.2–1.0)	0.5 (0.1–0.8)
	5–9 years	18.8 (17.9–19.8)	3.2 (2.8–3.6)	0.3 (0.2–0.4)	0.3 (0.2–0.4)
	10–14 years	10.3 (9.6–11.0)	1.4 (1.1–1.6)	0.2 (0.1–0.3)	0.2 (0.1–0.3)
	15–19 years	9.5 (8.8–10.1)	1.8 (1.5–2.0)	0.1 (0.0–0.2)	0.3 (0.1–0.4)
	20–24 years	9.6 (8.9–10.3)	2.4 (2.0–2.7)	0.1 (0.1–0.2)	0.2 (0.1–0.3)
	25–29 years	11.6 (10.9–12.4)	2.9 (2.5–3.2)	0.1 (0.0–0.1)	0.4 (0.3–0.5)
	30–34 years	14.9 (14.2–15.7)	4.4 (4.0–4.8)	0.2 (0.1–0.3)	0.6 (0.4–0.7)
	35–59 years	20.2 (19.4–21.0)	6.2 (5.8–6.7)	0.3 (0.2–0.3)	0.9 (0.7–1.1)
	40–44 years	28.5 (27.6–29.4)	7.9 (7.4–8.3)	0.3 (0.2–0.4)	0.9 (0.8–1.1)
	45–49 years	40.9 (39.8–41.9)	9.5 (9.0–10.0)	0.5 (0.4–0.6)	1.4 (1.2–1.6)
	50–54 years	58.4 (57.0–59.7)	11.3 (10.7–11.9)	0.6 (0.5–0.8)	1.8 (1.6–2.1)
	55–59 years	85.4 (83.7–87.1)	17.0 (16.3–17.8)	0.9 (0.7–1.1)	2.8 (2.5–3.2)
	60–64 years	117.3 (115.2–119.5)	23.9 (22.9–24.8)	1.5 (1.3–1.8)	3.8 (3.4–4.2)
	65–69 years	150.2 (147.7–152.8)	31.5 (30.3–32.7)	1.5 (1.3–1.8)	4.2 (3.8–4.7)
	70–74 years	184.6 (181.6–187.5)	38.4 (37.1–39.8)	1.5 (1.2–1.8)	5.3 (4.8–5.8)
	75–79 years	249.0 (245.2–252.9)	53.3 (51.5–55.1)	1.4 (1.1–1.7)	5.9 (5.3–6.5)
	80–84 years	334.5 (329.7–339.3)	82.2 (79.8–84.6)	1.2 (1.0–1.5)	8.1 (7.4–8.9)
	85–89 years	476.5 (470.0–483.0)	134.7 (131.3–138.2)	1.0 (0.7–1.3)	13.5 (12.4–14.6)
	≥90 years	615.6 (606.2–625)	197.1 (191.7–202.4)	0.7 (0.4–1.0)	17.9 (16.3–19.5)
Both	Total	108.9 (108.6–109.3)	25.4 (25.2–25.6)	0.7 (0.7–0.7)	3.5 (3.4–3.5)
	<1 year	185.4 (180.1–190.7)	8.1 (7.0–9.3)	3.4 (2.7–4.1)	4.0 (3.2–4.8)
	1.00 years	78.9 (75.5–82.2)	14.7 (13.2–16.1)	1.4 (1.0–1.8)	3.1 (2.5–3.8)
	2.00 years	56.3 (53.6–59.1)	12.1 (10.9–13.4)	1.2 (0.8–1.6)	1.6 (1.1–2.1)
	3.00 years	48.0 (45.5–50.5)	12.7 (11.4–13.9)	0.8 (0.5–1.1)	0.6 (0.3–0.9)
	4.00 years	36.9 (34.8–39.1)	8.4 (7.4–9.4)	0.8 (0.4–1.1)	0.7 (0.4–0.9)
	5–9 years	18.3 (17.6–18.9)	3.1 (2.8–3.4)	0.3 (0.2–0.4)	0.3 (0.2–0.4)
	10–14 years	10.8 (10.3–11.3)	1.3 (1.1–1.5)	0.2 (0.2–0.3)	0.2 (0.1–0.3)
	15–19 years	12.9 (12.4–13.5)	2.2 (2–2.5)	0.1 (0.0–0.2)	0.3 (0.3–0.4)
	20–24 years	12.4 (11.8–12.9)	2.5 (2.3–2.8)	0.1 (0.0–0.1)	0.3 (0.2–0.4)
	25–29 years	14.2 (13.6–14.7)	3.3 (3.0–3.6)	0.1 (0.1–0.2)	0.6 (0.4–0.7)
	30–34 years	18.5 (17.9–19.1)	5.0 (4.6–5.3)	0.3 (0.2–0.3)	0.8 (0.7–0.9)
	35–59 years	24.4 (23.8–25.0)	7.0 (6.6–7.3)	0.4 (0.3–0.4)	1.1 (0.9–1.2)
	40–44 years	33.83 (33.1–34.5)	9.4 (9–9.7)	0.5 (0.4–0.6)	1.4 (1.2–1.5)
	45–49 years	48.7 (47.8–49.5)	11.7 (11.3–12.2)	0.6 (0.5–0.6)	2.1 (1.9–2.3)
	50–54 years	73.1 (72.1–74.2)	15.3 (14.8–15.7)	0.7 (0.6–0.8)	2.6 (2.4–2.8)
	55–59 years	107.8 (106.4–109.1)	21.5 (20.9–22.1)	0.9 (0.8–1.0)	3.9 (3.7–4.2)
	60–64 years	155.3 (153.6–157.0)	5.4 (5.1–5.8)	1.4 (1.3–1.6)	5.4 (5.1–5.8)
	65–69 years	209.6 (207.4–211.8)	6.8 (6.4–7.2)	1.6 (1.4–1.8)	6.8 (6.4–7.2)
	70–74 years	269.5 (266.9–272.1)	8.4 (8.0–8.9)	1.6 (1.4–1.8)	8.4 (8.0–8.9)
	75–79 years	356.3 (352.9–359.7)	10.9 (10.3–11.5)	1.5 (1.3–1.7)	10.9 (10.3–11.5)
	80–84 years	461.3 (457.0–465.6)	12.7 (12.0–13.4)	1.3 (1.0–1.5)	12.7 (12.0–13.4)
	85–89 years	615.5 (609.5–621.4)	18.3 (17.3–19.3)	0.9 (0.7–1.2)	18.3 (17.3–19.3)
	≥90 years	748.0 (739.3–756.8)	241.6 (236.6–246.5)	0.6 (0.4–0.9)	22.0 (20.5–23.5)

*Differences statistically significant ($p < .05$) per sex.
**Differences statistically significant ($p < .05$) per age group.

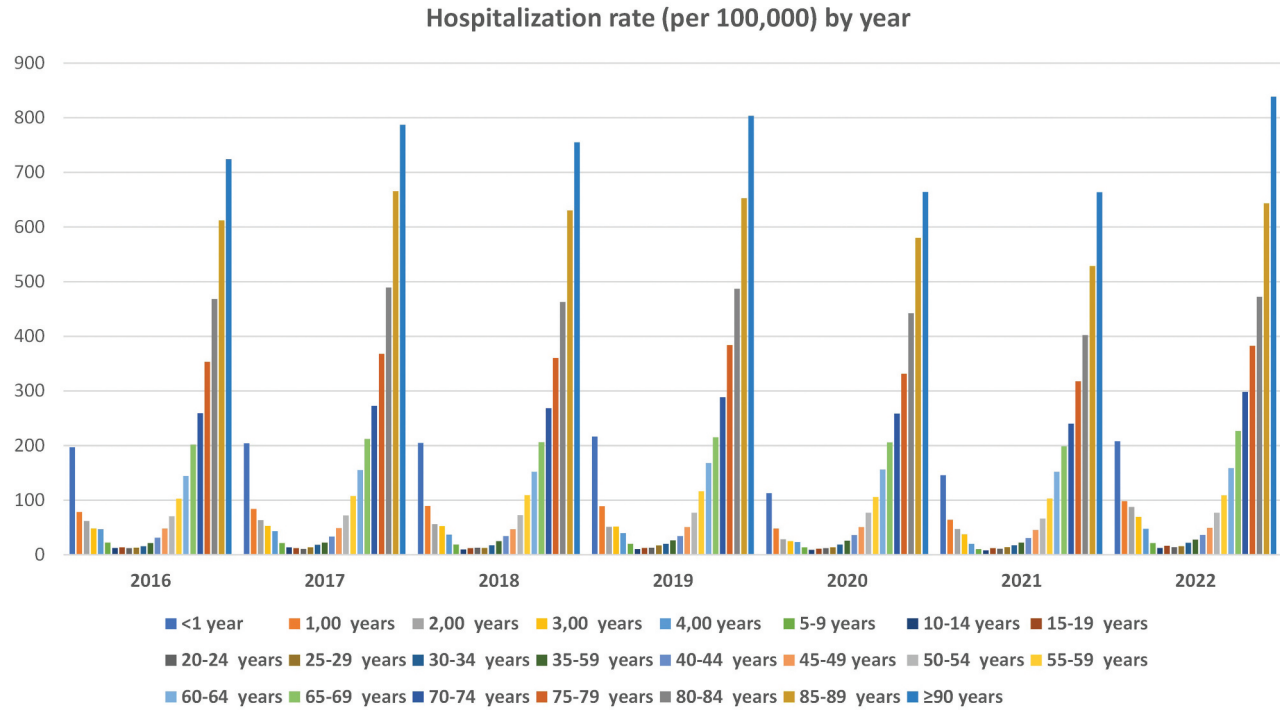

Figure 1. Hospitalization rate for pneumococcal disease in Spain by year (2016–2022).

($p < .05$) by year were found in hospitalization rates for pneumococcal disease in most age groups (Figure 1). Compared to 2019, the number of hospital infections for pneumococcal infection hospitalizations decreased by 18% in 2020 and 45% in 2021.

Among the cases identified 83,657 (23.3%) were pneumococcal pneumonia, 2,317 (0.7%) were meningitis, and 11,471 (3.2%) were sepsis. Thus, the total hospitalization rates were 25.4 (95% CI: 25.2–25.6), 0.7 (95% CI: 0.7–0.7), and 3.5 (95% CI: 3.4–3.5) per 100,000 people, respectively, with pneumococcal pneumonia having a higher rate than meningitis or sepsis (Table 1).

Pneumococcal pneumonia

Significant differences ($p < .05$) in hospitalization rates by sex were found for pneumococcal pneumonia, with higher rates in men than in children <1 year of age, especially for those older than 25 years of age (Table 1 and Figure 2). Significant

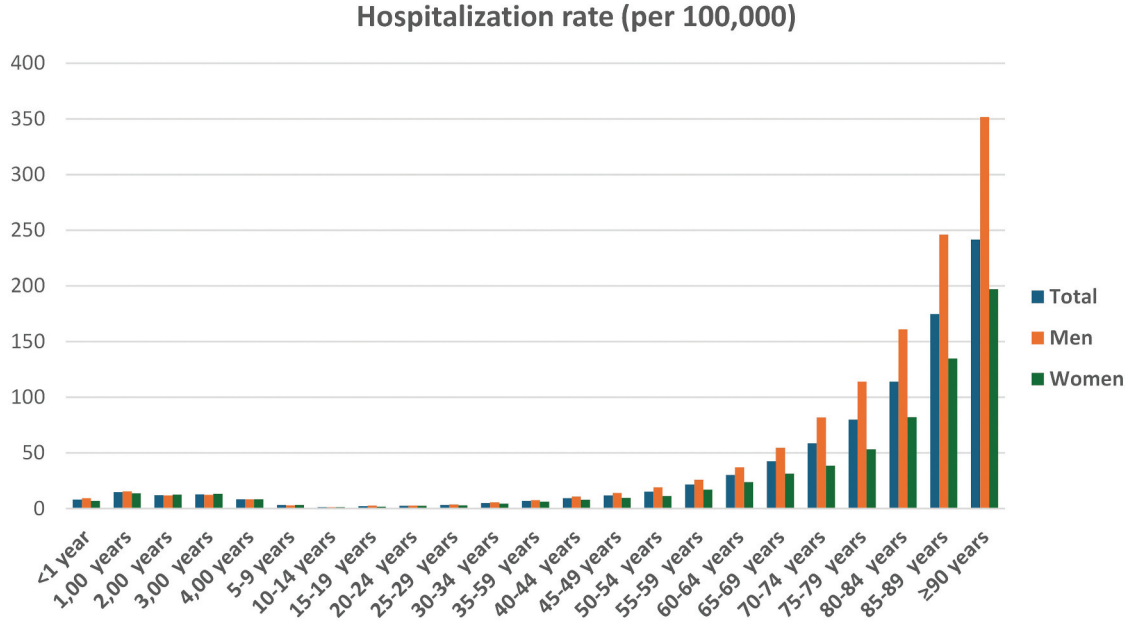

Figure 2. Hospitalization rate in Spain related to pneumococcal pneumonia according to sex and age.

differences ($p < .05$) in hospitalization rates were also found by year (data not shown). The median hospital stay was 6 days (IQR 6 days), with a mean cost of 5,319.6€ (SD: 7,352.2€) per hospitalization, resulting in a total annual cost of EUR 63.6 million.

Pneumococcal meningitis

Among meningitis cases, the highest hospitalization rate was reported in children <1 year old (3.4; CI 95%: 2.7–4.1). This ratio decreased and gradually rose again after age 30, reaching 1.6 (95% CI: 1.4–1.8) between the ages of 65–69, which is lower than in the youngest individuals (Table 1 and Figure 3). The differences by year were statistically significant ($p < .05$) (data not shown), especially in the age groups. The median hospital stay was 14 days (IQR 11 days), with a mean cost of 13,558.5€ (SD: 12232.2€) per hospitalization, resulting in a total annual cost of EUR 4.5 million.

Pneumococcal sepsis

According to the sepsis data, hospitalization rates increased with age, rising sharply from the age of 60 years (5.4; CI 95%: 5.1–5.8) to peak in those over 90 years of age (22.0; CI 95%: 20.5–23.5) (Table 1 and Figure 4). The mean cost of each hospital stay for this population was 9,529.2€ (SD: 12249.1€) for a median hospital stay of 9 days (IQR 11 days), reaching

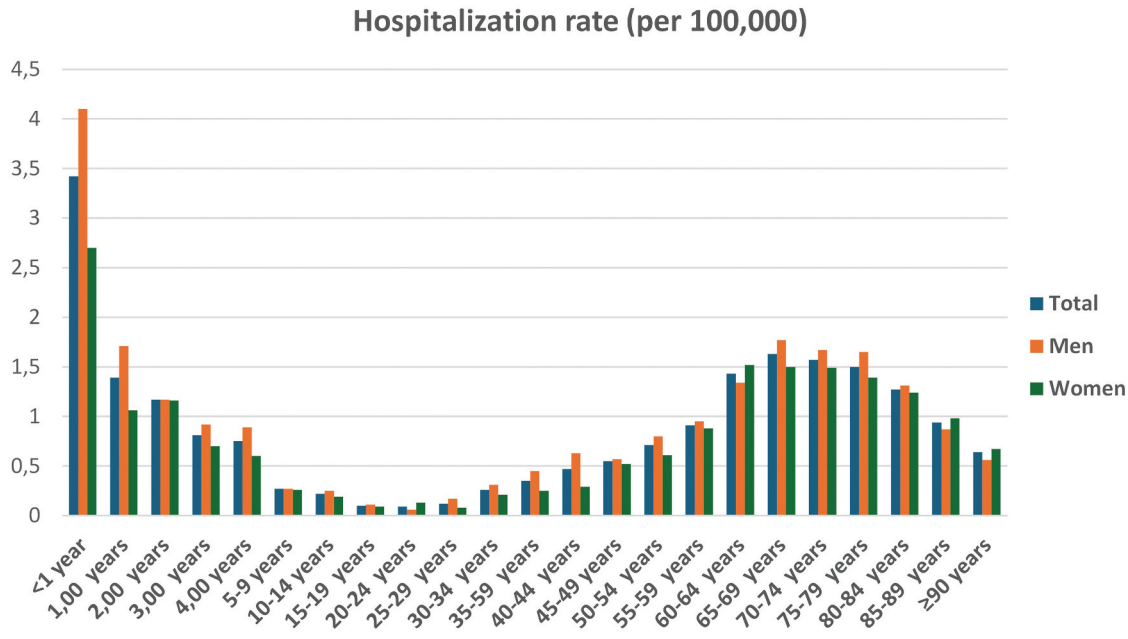

Figure 3. Hospitalization rate in Spain related to pneumococcal meningitis by sex and age.

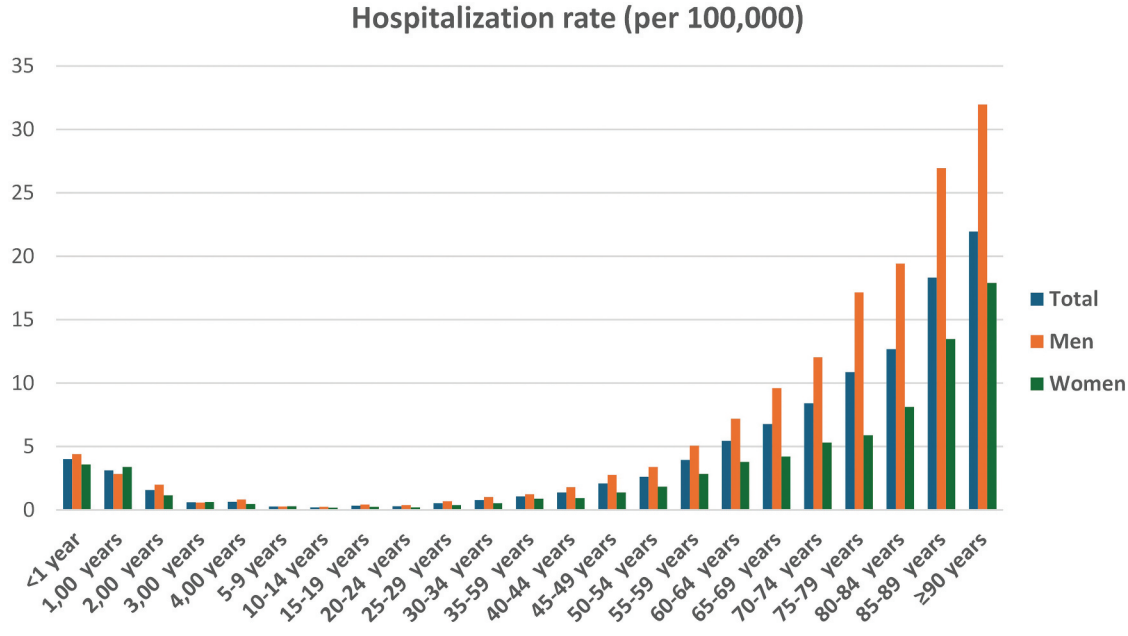

Figure 4. Hospitalization rate in Spain related to pneumococcal sepsis according to sex and age.

a total annual cost of EUR 15.6 million. Significant differences ($p < .05$) were also found by year after the age of 40 (data not shown).

Mortality

The total number of deaths among all hospitalized pneumococcal infection cases analyzed from 2016 to 2022 was 51,668, corresponding to a mortality rate of 15.7 (95% CI: 15.6–15.8) per 100,000 (Supplementary Table S1). The total case fatality rate was 14.4% (95% CI: 14.3–14.5) (Table 2).

The number of deaths among pneumococcal pneumonia patients was 6,593; among meningitis patients, 245; and 2,265 among sepsis patients. Thus, the mortality rates were 2 (95% CI: 1.95–2.05), 0.07 (95% CI: 0.06–0.08), and 0.69 (95% CI: 0.66–0.72) deaths per 100,000 people, respectively (Supplementary Table S1). The corresponding case fatality rates were 7.9% (95% CI: 7.7–8.1), 10.6% (95% CI: 9.3–11.8), and 19.8% (95% CI: 19.0–20.5), respectively (Table 2). Both mortality and case fatality rates were significantly higher ($p < .05$) in men (Supplementary Table S1 and Table S2). The mortality rate was higher for pneumococcal pneumonia than for meningitis or sepsis, but the case fatality rate was higher for sepsis.

Mortality (Supplementary Table S1) and case-fatality (Table 2) rates increased dramatically with age ($p < .05$) until they reached their maximum values in the ≥90 years of age population, with 160.44 deaths per 100,000 population (CI 95%: 156.4–164.5) and 21.5% (CI 95%: 21.0–21.9), respectively (Supplementary Table S1 and Table S2). For pneumococcal pneumonia and sepsis, the highest mortality rates were found in patients aged ≥80 years, whereas for meningitis, the highest mortality rates were found after 70 years of age (Supplementary Table S1). The highest case fatality rates were reached in the population over 90 years of age for pneumococcal pneumonia (15.5%; 95% CI: 14.7–16.2), meningitis (50%; 95% CI: 30–70), and sepsis (37.9%; 95% CI: 34.6–41.2). Case-fatality rates were higher for men, with significant differences ($p < .05$) between the sexes after 40 years of age (Table 2).

Comorbidities

A total of 358,603 cases of pneumococcal disease were recorded between 2016 and 2022. Most patients presented at least one underlying condition (87.8%). The largest risk group was cardiopulmonary disease (63.9%), followed by arterial hypertension (AHT) (48.5%), cancer (40.3%), neoplasms (32.2%), and essential AHT (31.8%). Case fatality rates among patients with at least one comorbidity were significantly higher ($p < .05$) than that among patients without underlying conditions (16.0% vs. 3.2%, respectively), with a fivefold greater probability of death (OR = 5.7; CI 95%: 5.4–6.1; Table 3) in those with associated comorbidities. The most critical risk factors for death were neoplasms (OR = 9.5), cerebrovascular disease (OR = 8.6), acute renal failure (OR = 8.5), solid tumors (OR = 8.5), and hepatic disease (OR = 6.79).

The case fatality rates in patients with at least one comorbidity were 9.0%, 14.0%, and 21.3% for pneumococcal pneumonia, meningitis, and sepsis, respectively, which were higher than those in patients with no comorbidity (2.6%, 3.7%, and 7.2%, respectively) (Table 3). The most important risk factors for the case fatality rate in patients with pneumococcal pneumonia were cerebrovascular disease (OR = 3.4), arterial hypertension (AHT) (OR = 2.98), essential AHT (OR = 1.9), chronic lower respiratory tract disease (OR = 1.7), acute renal failure (OR = 1.4), and diabetes (OR = 1.4). In cases of meningitis, the most important risk factors were renal failure (OR = 12.6), tobacco use (OR = 8.7), cerebrovascular disease (OR = 8.7), and neoplasms (OR = 7.4). According to the sepsis data, cerebrovascular disease (OR = 6.29), neoplasms (OR = 5.7), hepatic disease (OR = 5.4), cancer (OR = 4.56), and acute renal failure (OR = 4.2) were the most common morbidities.

Discussion

In this retrospective study, we updated the data on the burden of hospitalization for pneumococcal disease in Spain between 2016 and 2023. Our analysis revealed that the hospitalization rate for pneumococcal disease increased notably with age. The total hospitalization rate for pneumococcal pneumonia patients was higher than that for meningitis or sepsis patients. This contributes more than EUR 384 million annually to the cost of the Spanish health system. These findings confirm that pneumococcal disease is associated with high morbidity and mortality across a wide variety of disease presentations. Most patients presented at least one comorbidity, increasing the case fatality rate fivefold.

The hospitalization rate for pneumococcal disease remained constant compared to a recent study conducted between 2016 and 2020 in Spain, which reported 108.4 hospitalizations per 100,000 people.[3] However, the rate has decreased for patients aged ≥50 years. Our study presented a rate of 231.4 per 100,000 population, in contrast to the data reported by studies conducted between 2003 and 2007, which reported rates of 632.7 per 100,000 population.[15] In addition, the hospitalization rates observed for the clinical syndromes pneumococcal pneumonia and meningitis align with those reported in the 2016–2020 studies (29.1 per 100,000 and 0.8 hospitalizations per 100,000, respectively). These results correspond to the decreasing trend in the incidence of pneumococcal pneumonia reported over the last decade.[16] However, this rate has increased for sepsis (1.2 hospitalizations per 100,000)[3]. This increase in the rate of hospitalization has been reported in a previous study by Darbà et al., who also sought to study the characteristics of patients with a pneumococcal disease between 2008 and 2017 in Spain[16], and Georgalis et al., who compared pneumococcal disease hospitalization rates between PCV7 and PCV13 vaccination periods[11]. Thus, sepsis hospitalizations, especially in older adults, warrant special attention in the future.

The hospitalization rate in children ≤1 year of age was 185.4 cases per 100,000, similar to that reported between 2016 and 2020 (186 cases per 100,000).[3] These rates correspond to the decrease observed in the past decade following the introduction of the PCV13 vaccine. Invasive pneumococcal disease (IPD) cases decreased by 89% in children under 2 years of age and 88% in those between 2–5 years old from 2009 to 2019[7], confirming the vaccine's effectiveness.[6,7] This effect has also been observed in other countries. In Italy, a decrease in the hospitalization rate was reported between 2002 and 2014

Table 2. Case fatality rates by sex and age group due to pneumococcal disease, pneumococcal pneumonia, meningitis, and sepsis in Spain (2016–2022).

		Case-fatality Rate (%) (CI 95%)			
Sex	Age group	Pneumococcal disease**	Pneumococcal Pneumonia	Pneumococcal Meningitis	Pneumococcal Sepsis
Male	Total	14.7 (14.6–14.9)	8.2 (8.0–8.5)	11.0 (9.3–12.8)	19.2 (18.3–20.1)
	<1 year	2.3 (1.7–2.8)	1.6 (−0.6–3.9)	5.7 (−0.6–11.9)	3.5 (−1.3–8.3)
	1.00 years	1.7 (0.9–2.5)	0.9 (−0.4–2.2)	0 (0–0)	2.5 (−2.3–7.3)
	2.00 years	1.0 (0.3–1.6)	0 (0–0)	5.9 (−5.3–17.1)	0 (0–0)
	3.00 years	1.0 (0.3–1.7)	0 (0–0)	0 (0–0)	11.1 (−9.4–31.6)
	4.00 years	2 (0.8–3.2)	0 (0–0)	0 (0–0)	15.4 (−4.2–35.0)
	5–9 years	1.5 (0.9–2.1)	1.2 (−0.2–2.5)	0 (0–0)	8.7 (−2.8–20.2)
	10–14 years	1.8 (1.0–2.6)*	0 (0–0)	0 (0–0)	0 (0–0)
	15–19 years	4.1 (3.1–5.2)	1.3 (−0.2–2.9)	11.1 (−9.4–31.6)	2.9 (−2.7–8.4)
	20–24 years	4.0 (2.9–5.1)	1.4 (−0.2–2.9)	0 (0–0)	3.1 (−2.9–9.2)
	25–29 years	3.7 (2.8–4.7)	2.4 (0.8–4.0)	13.3 (−3.9–30.5)	3.2 (−1.2–7.5)
	30–34 years	4.1 (3.3–4.9)	1.2 (0.3–2.2)	3.1 (−3.0–9.2)	2.9 (−0.3–6.1)
	35–59 years	4.4 (3.7–5.0)*	1.5 (0.7–2.3)	1.8 (−1.7–5.3)	7.7 (3.5–12.0)
	40–44 years	5.9 (5.3–6.6)*	1.9 (1.2–2.3)	7.9 (2.3–13.5)	8.4 (4.9–11.8)
	45–49 years	8.5 (7.9–9.1)*	3.3 (2.5–4.1)*	12.8 (5.4–20.2)	10.3 (7.3–13.4)
	50–54 years	11.4 (10.9–12.0)*	5.6 (4.7–6.5)*	6.9 (2.0–11.9)	13.6 (10.3–16.8)
	55–59 years	13.5 (12.9–14.0)*	6.7 (5.8–7.6)*	6.5 (1.9–11.2)	17.6 (14.5–20.8)*
	60–64 years	15.4 (14.9–15.9)*	6.3 (5.5–7.1)*	6.3 (2.1–10.4)	16.0 (13.3–18.8)
	65–69 years	16.4 (15.9–16.8)*	7.2 (6.4–7.9)*	12.6 (7.2–18.0)	17.4 (14.8–20.1)
	70–74 years	16.1 (15.7–16.6)*	8.3 (7.6–9.0)*	22.6 (15.0–30.3)*	20.9 (18.1–23.6)
	75–79 years	16.9 (16.4–17.3)*	8.7 (8.0–9.4)*	11.9 (5.0–18.8)	22.2 (19.4–24.9)
	80–84 years	17.3 (16.8–17.8)*	10.1 (9.3–10.8)	32 (19.1–44.9)	24.5 (21.4–27.6)
	85–89 years	18.8 (18.3–19.3)*	12.3 (11.5–13.1)	57.1 (36.0–78.3)	30.6 (27.0–34.1)
	≥90 years	21.2 (20.5–22.0)	15.3 (14.2–16.5)	50 (10.0–90.0)	36.5 (31.4–41.6)
Female	Total	14.0 (13.8–14.2)	7.4 (7.2–7.7)	10.1 (8.3–11.9)	20.7 (19.5–21.9)
	<1 year	1.7 (1.1–2.3)	0 (0–0)	9.1 (−0.7–18.9)	9.1 (0.6–17.6)
	1.00 years	1.6 (0.9–2.4)	0 (0–0)	7.1 (−6.4–20.6)	6.7 (−0.6–14.0)
	2.00 years	0.7 (0.1–1.2)	0 (0–0)	0 (0–0)	6.3 (−5.6–18.1)
	3.00 years	0.7 (0.1–1.4)	0.5 (−0.5–1.6)	0 (0–0)	0 (0–0)
	4.00 years	0.9 (0.1–1.6)	0.8 (−0.8–2.3)	0 (0–0)	14.3 (−11.6–40.2)
	5–9 years	0.8 (0.3–1.2)	0 (0–0)	0 (0–0)	4.4 (−4.0–12.7)
	10–14 years	3.4 (2.2–4.6)	0.9 (−0.8–2.6)	6.3 (−5.6–18.1)	13.3 (−3.9–30.5)
	15–19 years	4.0 (2.6–5.4)	0 (0–0)	14.3 (−11.6–40.2)	0 (0–0)
	20–24 years	4.4 (3.0–5.9)	0.5 (−0.5–1.6)	10 (−8.6–28.6)	12.5 (−3.7–28.7)
	25–29 years	4.6 (3.4–5.9)	2.0 (0.3–3.6)	0 (0–0)	5.7 (−2.0–13.4)
	30–34 years	5.2 (4.0–6.3)	0.7 (−0.1–1.5)	9.5 (−3.0–22.1)	3.6 (−1.3–8.4)
	35–59 years	7.1 (6.1–8.1)	1.5 (0.6–2.3)	3.3 (−3.1–9.8)	6.5 (1.8–11.1)
	40–44 years	8.7 (7.8–9.6)	1.7 (0.9–2.5)	5 (−1.8–11.8)	7.1 (2.6–11.6)
	45–49 years	10.4 (9.6–11.2)	1.7 (1.0–2.5)	14.5 (6.2–22.8)	11.5 (6.9–16.1)
	50–54 years	12.6 (11.8–13.4)	3.4 (2.4–4.3)	7.7 (1.8–13.6)	15.4 (10.8–20)
	55–59 years	13.2 (12.6–13.9)	4.4 (3.5–5.3)	5.8 (1.3–10.4)	11.1 (7.8–14.5)
	60–64 years	13.2 (12.6–13.8)	4.1 (3.3–4.9)	4.6 (1.3–7.8)	12.5 (9.2–15.8)
	65–69 years	13.4 (12.8–14.0)	4.9 (4.1–5.7)	5.3 (1.5–9.1)	14.4 (10.9–18.0)
	70–74 years	13.3 (12.8–13.9)	4.7 (3.9–5.4)	8.3 (3.4–13.3)	21.0 (17.2–24.9)
	75–79 years	14.3 (13.8–14.8)	6.1 (5.3–6.9)	17.8 (9.9–25.7)	21.4 (17.3–25.5)
	80–84 years	15.8 (15.2–16.3)	9.3 (8.5–10.1)	15.7 (7.2–24.2)	26.6 (22.6–30.7)
	85–89 years	17.5 (17.0–18.0)	11.1 (10.3–11.9)	42.9 (27.9–57.8)	32.8 (29–36.6)
	≥90 years	21.6 (21.0–22.2)	15.6 (14.6–16.6)	50 (26.9–73.1)	38.9 (34.5–43.3)
Both	Total	14.4 (14.3–14.5)	7.9 (7.7–8.1)	10.6 (9.3–11.8)	19.8 (19.0–20.5)
	<1 year	2.0 (1.6–2.4)	1.0 (−0.4–2.3)	7.0 (1.6–12.4)	5.9 (1.3–10.6)
	1.00 years	1.7 (1.1–2.2)	0.5 (−0.2–1.2)	2.6 (−2.5–7.7)	4.7 (0.2–9.2)
	2.00 years	0.8 (0.4–1.3)	0 (0–0)	3.0 (−2.8–8.9)	2.2 (−2.1–6.5)
	3.00 years	0.9 (0.4–1.3)	0.3 (−0.3–0.8)	0 (0–0)	5.6 (−5.0–16.2)
	4.00 years	1.4 (0.7–2.1)	0.4 (−0.4–1.2)	0 (0–0)	15 (−0.6–30.7)
	5–9 years	1.2 (0.8–1.5)	0.6 (−0.1–1.)	0 (0–0)	6.5 (−0.6–13.7)
	10–14 years	2.5 (1.8–3.2)	0.4 (−0.4–1.3)	2.6 (−2.5–7.7)	5.4 (−1.9–12.7)
	15–19 years	4.1 (3.3–5.0)	0.8 (−0.1–1.8)	12.5 (−3.7–28.7)	1.8 (−1.7–5.4)
	20–24 years	4.2 (3.3–5.0)	1.0 (0.0–1.9)	6.7 (−6.0–19.3)	6.3 (−0.6–13.1)
	25–29 years	4.1 (3.3–4.9)	2.2 (1.0–3.4)	9.1 (−2.9–21.1)	4.1 (0.2–8)
	30–34 years	4.5 (3.9–5.2)	1.0 (0.4–1.6)	5.7 (−0.6–11.9)	3.1 (0.4–5.8)
	35–59 years	5.5 (4.9–6.1)	1.5 (1.0–2.0)	2.3 (−0.9–5.5)	7.2 (4.1–10.4)
	40–44 years	7.1 (6.6–7.6)	1.8 (1.3–2.3)	7.08 (2.6–11.4)	7.9 (5.2–10.7)
	45–49 years	9.3 (8.8–9.8)	2.7 (2.1–3.2)	13.6 (8.1–19.2)	10.7 (8.2–13.3)
	50–54 years	11.9 (11.4–12.4)	4.7 (4.1–5.4)	7.3 (3.5–11.1)	14.2 (11.6–16.9)
	55–59 years	13.4 (13.0–14.0)	5.8 (5.1–6.4)	6.2 (2.9–9.5)	15.3 (12.9–17.6)
	60–64 years	14.5 (14.1–14.9)	5.4 (4.9–6.0)	5.3 (2.7–7.9)	14.7 (12.6–16.9)
	65–69 years	15.2 (14.9–15.6)	6.3 (5.7–6.9)	9.1 (5.7–12.5)	16.5 (14.3–18.6)
	70–74 years	15.1 (14.7–15.4)	7.0 (6.6–7.6)	15.3 (10.7–19.9)	20.9 (18.7–23.2)
	75–79 years	15.9 (15.5–16.2)	7.7 (7.2–8.3)	14.9 (9.6–20.2)	21.9 (19.6–24.2)
	80–84 years	16.6 (16.3–17.0)	9.7 (9.2–10.3)	22.5 (15.0–30.0)	25.3 (22.9–27.8)
	85–89 years	18.1 (17.8–18.5)	11.7 (11.1–12.3)	47.6 (35.3–60.0)	31.6 (29.0–34.2)
	≥90 years	21.5 (21.0–22.0)	15.5 (14.7–16.2)	50 (30–70)	37.9 (34.6–41.2)

*Differences statistically significant ($p < .05$) per sex.
**Differences statistically significant ($p < .05$) per age group.

Table 3. Case fatality rates and ODD ratios according to risk factors for pneumococcal disease, pneumococcal pneumonia, meningitis, and sepsis in Spain (2016–2022).

	Pneumococcal disease		Pneumococcal Pneumonia		Pneumococcal Meningitis		Pneumococcal Sepsis	
Comorbidity	ODDs ratio	Case-fatality rate (%)	ODDs ratio	Case-fatality rate (%)	ODDs ratio	Case-fatality rate (%)	ODDs ratio	Case-fatality rate (%)
No risk group	1	3.2	1	2.6	1	3.7	1	7.2
Risk group	5.7 (5.4–6.1)	16.0	4.8 (4.7–4.9)	9.0	4.3 (2.8–6.4)	14.0	3.5 (2.8–4.3)	21.4
HIV	3.4 (3.0–3.9)	10.1	0.1 (0.1–0.1)	5.0	5.8 (1.9–18.3)	18.2	3.0 (2.0–4.5)	19.1
Cancer	8.5 (8.0–9.0)	22.0	1.1 (1.1–1.2)	12.6	4.6 (3.0–7.2)	14.9	4.6 (3.7–5.7)	26.2
Neoplasms	9.5 (9.0–10.1)	24.0	0.6 (0.6–0.7)	14.2	7.4 (4.4–12.7)	22.0	5.7 (4.5–7.3)	30.8
Immunosuppression	4.1 (3.7–4.7)	12.0	0.07 (0.07–0.08)	9.1	1.1 (0.1–8.4)	4.0	2.6 (1.7–4.0)	16.8
Diabetes	5.5 (5.2–5.9)	15.5	1.4 (1.4–1.4)	8.7	4.1 (2.6–6.5)	13.5	3.6 (2.9–4.5)	21.9
AHT essential	5.1 (4.8–5.4)	14.4	1.9 (1.9–1.9)	8.0	3.3 (2.1–5.1)	11.2	3.3 (2.6–4.1)	20.3
AHT diseases	5.5 (5.2–5.8)	15.3	2.9 (2.8–2.9)	9.0	3.6 (2.3–5.5)	12.0	3.7 (2.9–4.6)	22.1
Cardiopulmonary disease	6.1 (5.8–6.5)	16.7	3.4 (3.4–3.5)	10.3	5.4 (3.6–8.2)	16.8	3.8 (3.1–4.7)	22.9
Chronic lower respiratory tract disease	4.0 (3.8–4.3)	11.8	1.7 (1.7–1.8)	6.4	4.0 (2.3–7.1)	13.2	2.4 (1.9–3.1)	15.9
Cerebrovascular disease	8.6 (8.0–9.1)	21.9	0.3 (0.3–0.3)	14.6	8.7 (5.4–14.2)	24.7	6.2 (4.7–8.1)	32.5
COPD	4.8 (4.5–5.1)	13.7	0.97 (0.95–0.99)	7.1	4.0 (1.9–8.4)	13.3	2.6 (2.0–3.4)	16.9
Asthma	2.7 (2.5–2.9)	8.2	0.4 (0.4–0.4)	4.1	3.0 (1.3–6.8)	10.3	2.3 (1.7–3.1)	15.1
Acute Renal Failure	8.5 (8.1–9.0)	22.0	1.4 (1.4–1.5)	13.7	12.6 (7.9–20.1)	32.4	4.2 (3.4–5.2)	24.6
Hepatic disease	6.7 (6.2–7.2)	18.1	0.2 (0.1–0.2)	11.7	5.6 (2.215–14.7)	17.7	5.4 (4.1–7.2)	29.5
Tobacco use	4.8 (4.0–5.6)	13.6	0.02 (0.02–0.02)	4.2	8.7 (2.2–34.0)	25.0	1.9 (0.8–4.7)	13.0

AHT: arterial hypertension; COPD: chronic obstructive pulmonary disease; HIV: Human immunodeficiency virus.

(29.1%)[17] and between 2012 and 2018[18] in vaccinated children. Similarly, in Israel, hospitalization rates have declined since the introduction of PCV in the pediatric population.[19] Similar results were observed in studies conducted in Japan.[20] and France[21] However, despite the decrease in hospitalization rates in children in Spain and other countries, no parallel reduction in this ratio has been observed in the older population. In Spain, de Miguel et al. reported that the disease burden by all serotypes in adults remained unchanged when comparing the pre-vaccine period (2009) and the last period studied (2019).[6,7] They reported 67% and 50% decreases in PCV13 serotype cases between 2009 and 2019 in adults aged 18–64 and those aged ≥65 years, respectively, thus confirming the benefit of herd immunity to the vaccine for the PCV13 serotypes in the adult population[7]. Another Spanish study focusing on CAP reported similar results between 2016 and 2018[22]. The multiple vaccine changes over the last two decades and the geographic diversity of pneumococcal serotypes worldwide make international comparisons challenging. However, other European countries that use the same vaccine schedule (2 + 1) as Spain have also observed serotype replacement by non-PCV13 serotypes.[21,23–25]

Although this study was not designed to assess the impact of current preventive measures on the population, the findings underline the importance of maintaining and using conjugate vaccines with high serotype coverage and reinforcing vaccination policies. New PCVs with a broader spectrum are currently being marketed (PCV15 and PCV20), and new vaccines are being developed (PCV21, PCV24, and PCV26). Thus, the NeumoExperts Prevention Group (NEP) in Spain[26] recommends that PCVs play a key role in preventing pneumococcal disease. However, considering new PCV vaccines cover most current pneumococcal diseases in Spain, using a single dose of PCV vaccine would facilitate compliance and avoid interference with future PCVs.[6] Additionally, the Sociedad Española de Medicina Preventiva, Salud Pública y Gestión Sanitaria (SEMPSPGS) makes similar recommendations.[27] In the US, the Advisory Committee on Immunization Practices (ACIP) also recommends the use of either PCV21, PCV20, or PCV15 for adults ≥65 years of age, for risk groups who have not previously received a pneumococcal conjugate vaccine and for those whose previous vaccination history is unknown.[28]

The hospitalization rate for pneumococcal disease in this study significantly differed by year in most age groups, likely due to the decrease in hospitalization rates during the COVID-19 pandemic in 2020 and 2021. Hospitalization rates rose again in 2022 to levels comparable to those reported from 2016– to 2019. This phenomenon was also observed in the US (46% decrease in 2020)[29] and Switzerland.[30] Casanova et al. also reported that IPD numbers began to increase in 2021 with the loosening of COVID-19 restrictions.[30] However, it is essential to note that during the COVID-19 pandemic, there was also an increase in resistant non-PCV13 serotypes, likely due to the widespread antibiotic use in patients infected with SARS-CoV-2.[31] The 11A and 24F serotypes are the most prevalent and have shown reduced susceptibility to penicillin and other β-lactams in Spanish adults.[31] The observed prevalence of non-PCV13 serotypes in adults and the increase in antibiotic-resistant serotypes highlight the importance of reinforcing vaccination with broad-spectrum PCVs in the Spanish population.

Our study identified the most critical risk factors that impact the case fatality rate in pneumococcal disease were neoplasms (OR = 9.5), cerebrovascular disease (OR = 8.6), acute renal failure (OR = 8.5), solid tumors (OR = 8.5), and cirrhosis (OR = 6.79). However, depending on the clinical manifestation, the most critical risk factor and the odds ratio can vary. Thus, for pneumococcal pneumonia, cerebrovascular disease (OR = 3.4) was the most crucial risk factor, while for meningitis, it was renal failure (OR = 12.6), and for sepsis, cerebrovascular disease (OR = 6.2). The presence of at least one comorbidity increased the case fatality rate fivefold in patients compared to those with no morbidity (16.0% vs. 3.2%, respectively). Importantly, we did not evaluate the ODD ratio in patients with more than one comorbidity, a common condition, particularly in elderly individuals. Thus, the odds ratios in this study (for individual risk conditions) could be higher due to associated comorbidities. In addition, a previous study reported that the CAP rate increased with the accumulation of risk factors and age in primary care. Thus, the risk associated with 1 risk factor was 1.4 in 18–60-year-old patients vs. 1.6 in those >60 years of age; with 2 risk factors, it was 1.9 vs. 2.4, and for ≥ 3 risk factors, it was 3.1 vs. 4.3.[32] These results emphasize the recommendation of pneumococcal vaccination not only in older adults but also in risk groups among immunocompetent adults to prevent disease and reduce complications.

From 2016 to 2022, pneumococcal disease cost our healthcare system 2,686 million EUR (more than 383 million EUR annually), which corresponds to a mean cost of 7,490.74€ per hospitalization, similar to the mean cost/hospitalization reported in previous studies[3,4,15,16,33] in Spain. The costs of pneumococcal pneumonia, meningitis, and sepsis were EUR 445 million, EUR 31.4 million, and EUR 109.3 million, respectively. These findings indicate that despite the use of PPV23 in the elderly population and the introduction of PCV13 into the pediatric vaccination calendar in 2016, pneumonia continues to represent a significant economic burden for our country.

This study has several limitations. Because we used the MBDS information system (which encodes hospital admissions), there could be redundant data related to patients hospitalized more than once during the study period. Thus, we could have overestimated the disease prevalence and underestimated its lethality. Furthermore, since the MBDS encodes hospital admissions, we did not consider cases managed in primary care or microbiological confirmation. Thus, we could have underestimated the actual impact of the disease. However, the MBDS is one of the most valuable clinical and epidemiological research tools. With the large number of records it contains, it is quite unlikely that a small amount of redundant data will affect the overall trend of the results. In fact, using this system is one of the strengths of this study because of its large sample size, which provides high representativeness and statistical power when analyzing clinical variables such as the case fatality rate. Furthermore, the MBDS is subject to a high-quality data audit at the state level.[34]

On the other hand, using a nationwide hospital database means that the reliability depends on the quality of the discharge reports and the precision of the ICD-10 codes

used to detect cases of pneumococcal infection.[35] We began transitioning from ICD-9-CM to ICD-10-CM in 2016, which may have impacted the epidemiological analysis, thus affecting the comparison of our hospitalization and mortality data with those previously published by this research group. Long-term epidemiological data are needed to assess the consequences of this transition.[36]

Another strength of this study is the seven-year collection period (2016–2022), starting in the year PCV13 became part of the public vaccination schedule for the pediatric population. Therefore, we are already collecting information influenced by vaccination, which will allow us to determine the future impact of immunization.

Conclusion

Our study confirmed that pneumococcal disease continues to be a major concern in our country in terms of hospitalization rate, morbidity, and mortality, especially in children and elderly individuals, resulting in a great expense to our health system. The introduction of PCV13 for childhood vaccination programs has led to a significant decrease in the number of new cases detected in this population worldwide, and the number of cases caused by PCV13-included serotypes in adults has also decreased because of herd immunity. In addition, the expected presence of comorbidities in the older population increases the severity of pneumococcal disease. There is a need for pneumococcal disease prevention mechanisms, especially in the elderly. Using new broad-spectrum PCVs and improving vaccination protocols for the elderly would help solve the existing problem.

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Author contributions

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship of this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

RGP: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing

VHB: Data curation, Formal Analysis, Methodology, Writing – review & editing

PMG: Conceptualization, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing

AGE: Conceptualization, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing

AGM: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing – original draft, Writing – review & editing.

Data availability statement

The anonymized datasets used in the current publication are available from the corresponding author upon reasonable request.

Ethics/Ethical approval

This study was performed in accordance with the principles of the Declaration of Helsinki of 1964. The Rey Juan Carlos University Ethics Committee determined that ethical approval for this study was not required.

Notes on contributor

Dr. Ruth Gil Prieto is a Preventive Medicine and Public Health professor at Rey Juan Carlos University in Madrid. Trained as a biochemist, she completed her PhD in epidemiology and public health. Because of her interest in humanitarian medicine and development, she quickly turned her attention to infectious disease epidemiology, particularly vaccines. After serving as an adjunct professor, she completed research stays in the pharmaceutical industry, closely following the clinical development of several vaccines. In 2010, she obtained her Tenure at the University Rey Juan Carlos (URJC) Madrid, where she taught epidemiology and served 7 years as the director of the International Cooperation and Volunteering Program. She leads the consolidated research group in epidemiology and the diagnosis of infection. She was also a visiting associate professor at the Department of Population Medicine, Harvard Medical School, in Boston, where her research focused on vaccine safety.

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