Journal of Infection 89 (2024) 106204

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Bacteria and Bacterial Diseases

Surveillance of invasive pneumococcal disease in Spain exploring the impact of the COVID-19 pandemic (2019-2023)

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ARTICLE INFO

Article history:
Accepted 11 June 2024
Available online 19 June 2024

Keywords:
S. pneumoniae
IPD
COVID-19
PCVs
Serotype 3
Serotype 4

SUMMARY

Objectives: Dynamic trends of invasive pneumococcal disease (IPD) including the evolution of prevalent serotypes are very useful to evaluate the impact of current and future pneumococcal conjugate vaccines (PCVs) and the rise of non-vaccine serotypes. In this study, we include epidemiological patterns of *S. pneumoniae* before and after COVID-19 pandemic.

Methods: We characterized all national IPD isolates from children and adults received at the Spanish Pneumococcal Reference Laboratory during 2019–2023.

Results: In the first pandemic year 2020, we found a general reduction in IPD cases across all age groups, followed by a partial resurgence in children in 2021 but not in adults. By 2022, IPD cases in children had returned to pre-pandemic levels, and partially in adults. In 2023, IPD rates surpassed those of the last pre-pandemic year. Notably, the emergence of serotype 3 is of significant concern, becoming the leading cause of IPD in both pediatric and adult populations over the last two years (2022–2023). Increase of serotype 4 in young adults occurred in the last epidemiological years.

Conclusions: The COVID-19 pandemic led to a temporary decline in all IPD cases during 2020 attributable to non-pharmaceutical interventions followed by a subsequent rise. Employing PCVs with broader coverage and/or enhanced immunogenicity may be critical to mitigate the marked increase of IPD.

Introduction

Prevention of invasive pneumococcal disease (IPD) in children and adults is one of the leading priorities worldwide as it is associated with high morbidity and mortality rates worldwide.[1,2] Implementation of pneumococcal conjugate vaccines (PCVs) are cost-effective measures and a very useful prophylactic strategy to prevent IPD and reduce the impact of antibiotic resistance.[3–6] In Spain, PCV13 was introduced in 2016 in the national immunization

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https://doi.org/10.1016/j.jinf.2024.106204

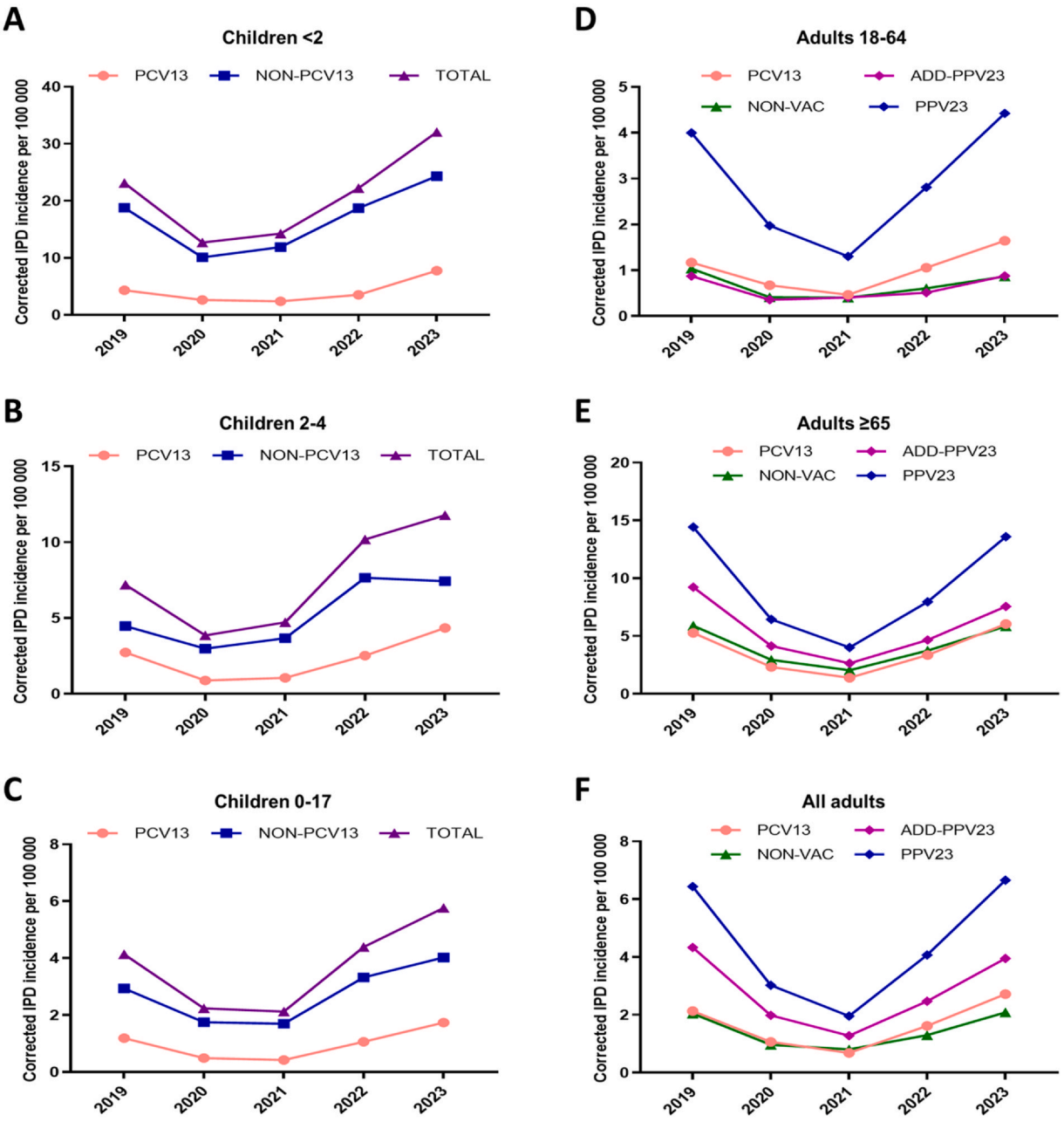


Fig. 1. Corrected annual incidence of IPD in Spain in pediatric and adult populations including pre-COVID-19 and COVID-19 periods (2019–2023). Data show IPD cases and incidence rates for < 2 years (A) 2–4 years (B) 0–17 years (C) 18–64 years (D) ≥65 years (E) and all adults ≥18 years (F). PCV13 represents the IPD cases by serotypes included in the 13-valent conjugate vaccine (pink line with dots). NON-PCV13 represents the IPD cases by serotypes that are not included in the 13-valent conjugate vaccine (blue dotted line with squares). Total represents all the IPD cases in the correspondent age group (purple line with triangles). Add-PPV23 (2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, and 33F) represent the IPD cases by additional serotypes included in PPV23 but not in PCV13 (purple dotted line with diamonds). NON-VAC represents all the IPD cases by serotypes that are not included in PCV13 and PPV23 (green line with triangles).

pediatric vaccine program (2+1 schedule), although it had been used in the private market with high coverage rates since 2010 ranging from 67–82%.[7,8] Vaccination coverage in children with PCV13 during the pre-pandemic/pandemic periods achieved > 95–97% (https://pestadistico.inteligenciadegestion.sanidad.gob.es/publicoSNS/I/sivamin/informe-de-evolucion-de-coberturas-de-vacunacion-por-vacuna). In immunocompetent adults aged ≥65 years old, the use of PPV23 was the general recommendation by the Spanish Ministry of Health since 2004 although several regions started using PCV13 for adults since 2016. In the last months of 2023, certain Spanish regions have recommended the use of PCV20 for immunocompetent adults. Vaccination coverage in adults aged ≥65 years old was much lower compared to children: 23.2%–29% with PCV13 and 18%–26.5% with PPV23 (data supplied from Spanish Ministry of Health).

In Spain, the use of PCVs during the pre-pandemic period has demonstrated a marked reduction of IPD by vaccine serotypes, including those associated with antimicrobial resistance.[6,7] The rise of non-PCV13 serotypes in the last years before the COVID-19 pandemic, affecting in great extent to the adult population was worrisome. The implementation of vaccines with higher serotype coverage in routine immunization schedules could counteract the possible emergence of non-PCV13 serotypes.[9,10]

The COVID-19 pandemic in 2020 and the introduction of non-pharmaceutical interventions (NPIs) such as facial masks, social

Table 1
Number of cases and corrected incidence of invasive pneumococcal disease in 2022–2023 compared with 2019 and 2020–2021.

	2019		2020-21		2022-23		IRR 2020-21 vs 2019	95% CI	IRR 2022-23 vs 2019	95% CI	IRR 2022-23 vs 2020-21	95% CI
	Cases	Corrected incidence (per 100 000)	Cases	Corrected incidence (per 100 000)	Cases	Corrected incidence (per 100 000)						
< 2 years old	139	23.10	151	13.45	290	27.10	0.58	0.46-0.73	1.17	0.96-1.44	2.01	1.65-2.45
PCV13	26	4.33	28	2.50	60	5.61	0.58	0.34-0.98	1.30	0.82-2.06	2.25	1.44-3.52
NON-PCV13	113	18.79	123	10.96	230	21.49	0.58	0.45-0.75	1.14	0.91-1.43	1.96	1.58-2.44
2-4 years old	74	7.19	84	4.28	196	10.96	0.60	0.44-0.81	1.52	1.17-1.99	2.56	1.98-3.31
PCV13	28	2.73	19	0.96	61	3.41	0.36	0.2-0.64	1.25	0.8-1.96	3.52	2.11-5.9
NON-PCV13	46	4.48	65	3.31	135	7.55	0.74	0.51-1.08	1.69	1.21-2.36	2.28	1.7-3.06
18-64 years old	1159	4.88	970	2.04	2091	4.33	0.42	0.38-0.45	0.89	0.83-0.95	2.13	1.98-2.3
PCV13	278	1.18	271	0.56	653	1.35	0.48	0.41-0.57	1.16	1-1.33	2.38	2.07-2.74
PPV23	949	4.00	783	1.64	1751	3.63	0.41	0.37-0.45	0.91	0.84-0.98	2.21	2.03-2.41
ADD-PPV23	674	2.84	517	1.09	1102	2.29	0.38	0.34-0.43	0.80	0.73-0.88	2.11	1.9-2.34
NON-VAC	207	0.88	182	0.38	336	0.70	0.44	0.36-0.53	0.80	0.67-0.95	1.83	1.52-2.19
≥65 years old	1477	20.39	1152	7.71	2430	15.64	0.38	0.35-0.41	0.77	0.72-0.82	2.03	1.89-2.17
PCV13	382	5.28	277	1.85	731	4.70	0.35	0.3-0.41	0.89	0.79-1.01	2.54	2.21-2.91
PPV23	1045	14.43	778	5.21	1679	10.81	0.36	0.33-0.4	0.75	0.69-0.81	2.07	1.9-2.26
ADD-PPV23	668	9.23	504	3.38	951	6.13	0.37	0.33-0.41	0.66	0.6-0.73	1.81	1.63-2.02
NON-VAC	427	5.89	371	2.49	746	4.80	0.42	0.37-0.48	0.81	0.72-0.92	1.93	1.71-2.19
TOTAL	2910	7.74	2409	3.18	5177	6.75	0.41	0.39-0.43	0.87	0.83-0.91	2.12	2.02-2.23

distancing, and the lockdown that the population suffered from March to June in Spain clearly affected the transmission of pneumococcal strains. During the first two years of the COVID-19 pandemic, a general reduction of IPD cases has been recently reported in several countries worldwide with an increasing trend by the end of 2021.[11]

In this study, we have included age-specific and serotype-specific trends in IPD in Spain for the last 5 years (2019–2023) in children and adults to evaluate the contribution of pneumococcal vaccines and the COVID-19 pandemic to the epidemiology of this disease.

Methods

Study design

In this study, we have performed a prospective observational national surveillance study that included all IPD isolates (10,496) reported by hospital laboratories to the Spanish Pneumococcal Reference Laboratory (SPRL) during the period 2019–2023.

The SPRL notifies every year to the European Center for Disease Control (ECDC) all the IPD cases in Spain, which cover up to 80 % of the national level according to estimates by the National Center for Epidemiology, and since 2018 notifies the cases to the Invasive Respiratory Infection Surveillance Network (IRIS). Serotyping was performed using Quellung reaction, dot blot assay using specific antisera, and/or PCR-capsular sequence typing.[6,7]

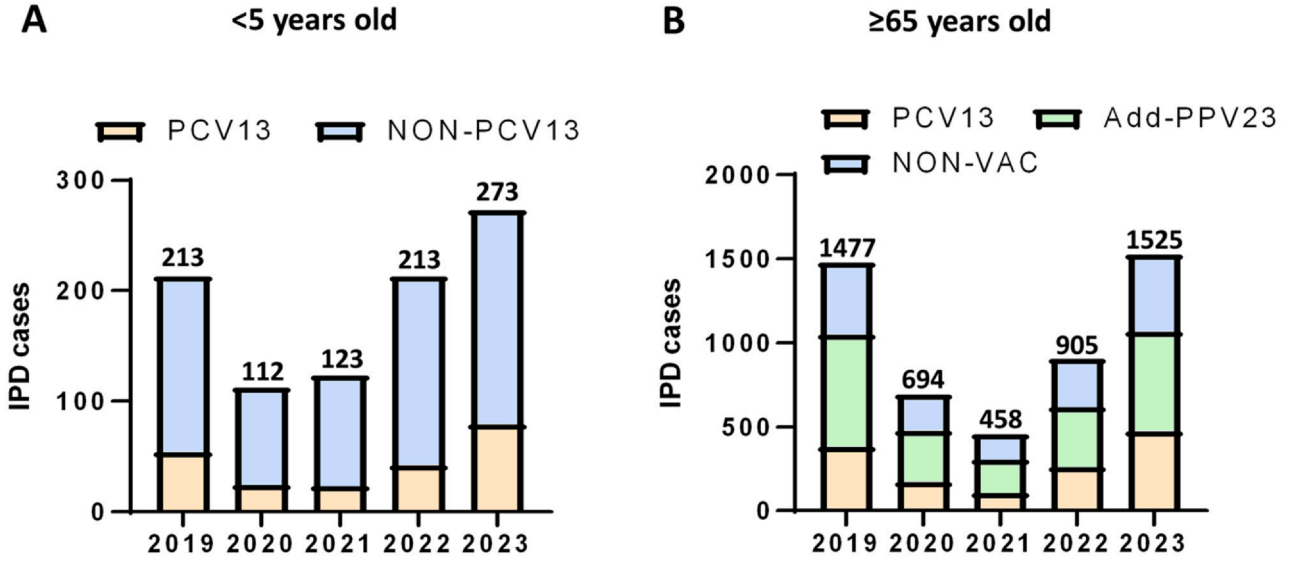
Data processing

The epidemiological year considered in the manuscript is from January to December. Serotypes were grouped into different categories depending on the population (pediatric or adults). For pediatric population, we considered as total (all serotypes), PCV13 serotypes and non-PCV13 serotypes. For adults, we considered PCV13 serotypes, additional PPV23 serotypes (those that are included in PPV23 but not in PCV13), PPV23 serotypes and non-vaccine serotypes (serotypes not included in PCV13 or PPV23). IPD evolution was analyzed for different age groups covering the pediatric population (< 2 years, 2–4 years, 0–17 years) and the adult population (18–64 years, ≥65 years, all adults). Incidence rate ratios (IRR) were analyzed comparing different periods. To analyze serotype distribution in the last epidemiological year with full data (2023), we included different age groups in children (< 2 years, 2–4 years and 5–17 years) and adults (18–64 years, 65–79 years and ≥80 years).

Potential serotype coverage by the different vaccines (PCV13, PCV15, PCV20, PCV21, PCV24) was evaluated in children < 5 years old and adults aged ≥65 years old for the period 2020–2023. We also assessed the potential coverage of the 23-valent polysaccharide vaccine (PPV23) for the adult population. Serotypes included in each vaccine are shown in Supplementary Fig. S1.

Statistical analysis

The observed incidence was calculated as the number of IPD episodes per 100,000 population and year using population data from the Spanish National Statistical Institute as denominator (Supplementary Fig. S2). The corrected incidence was calculated by applying the population capture of 80% to the denominator. We analyzed the evolution of IPD after the COVID-19 pandemic. Comparison of different periods were analyzed by calculating the incidence rate ratio (IRR) using Poisson regression models. Statistical analyses were performed using STATA v.14.



	TOP 3 SEROTYPES (N; %)		
2019	**24F** (28;13.2%)	**3** (21;9.9%)	**8** (19;8.9%)
2020	**24F** (18;16.1%)	**19A** (11;9.8%)	**15B** (10;8.9%)
2021	**24F** (19;15.5%)	**10A** (12;9.8%)	**23B** (10;8.1%)
2022	**24F** (31;14.6%)	**3** (28;13.2%)	**10A** (21;9.9%)
2023	**3** (47;17.2%)	**24F** (44;16.1%)	**22F** (20;7.3%)

	TOP 3 SEROTYPES (N; %)		
2019	**8** (269;18.2%)	**3** (199;13.5%)	**22F** (77;5.21%)
2020	**8** (122;17.6%)	**3** (84;12.1%)	**9N** (34;4.9%)
2021	**8** (85;18.6%)	**3** (63;13.8%)	**6C** (35;7.6%)
2022	**3** (162;17.9%)	**8** (152;16.8%)	**22F** (50; 5.52%)
2023	**3** (325;21.3%)	**8** (230;15.1%)	**22F** (103;6.8%)

Fig. 2. Dynamics showing the resurgence of IPD comparing the period 2019–2023. Data show IPD cases by PCV13 serotypes (orange), non-PCV13 serotypes (blue) in children < 5 years old including the three most prevalent serotypes of each year (A). Data show IPD cases by PCV13 serotypes (orange), additional serotypes covered by PPV23 (green), and non-vaccine serotypes (blue) in adults aged ≥65 years old including the three most prevalent serotypes of each year (B).

Results

Evolution of IPD in pediatric and adult population

During the first pandemic year 2020, there was a marked reduction of IPD cases in the age group < 2 years old (IRR, 0.58; 95% CI, 0.46–0.73) followed by a partial rise in the second year (2021) (Fig. 1A-C and Table 1). However, in 2022/2023 coinciding with the end of NPIs, we observed a full resurgence to pre-pandemic levels in 2019 (IRR, 1.17; 95% CI, 0.96–1.44); Fig. 1A-C and Table 1). A similar epidemiological pattern was confirmed in other pediatric age groups analyzed (Fig. 1B,C and Table 1). Data from 2023 confirmed the complete resurgence of IPD cases to pre-pandemic levels (Fig. 1A-C).

During the first two pandemic years (2020/2021), there was a substantial reduction of IPD cases affecting all serotypes (IRR, 0.38; 95% CI, 0.35–0.41 for the age group ≥65 years old and IRR, 0.42; 95% CI, 0.38–0.45 for adults aged 18–64 years old, Fig. 1D-F and Table 1). In 2022, we observed a partial increase in IPD incidences, although at lower levels than the last pre-pandemic year 2019, whereas in 2023, the resurgence was complete (Fig. 1D-F and Table 1).

Impact of COVID-19 in the distribution of serotypes causing IPD in Spain

The appearance of the pandemic had a clear impact not only on the burden of disease but also in the distribution of serotypes causing IPD (Fig. 2). In children < 5 years, we observed a 48% reduction in 2020 (213 cases in 2019 vs 112 cases in 2020) mainly attributable to the implementation of NPIs followed by an increase in IPD cases in the following years (123 cases in 2021, 213 in 2022 and 273 cases in 2023) obtaining even higher levels with the last pre-pandemic year. The distribution of serotypes was variable between the different years except serotype 24F, whose presence was constant among the three most prevalent serotypes during the five years evaluated (Fig. 2A). Other prevalent serotypes among the 10 most frequent during the period 2020–2023 were serotypes 3, 8, 10A, and 15B (Supplementary Table 1). In 2023, we observed an important increase of serotype 3 (21 cases in 2019 vs 47 cases in 2023) and serotype 24F (28 cases in 2019 vs 44 cases in 2023). A large proportion of IPD cases by serotype 3 in children < 2 years (70%) were in children < 2 months (30%; age before starting vaccination schedule) or in children aged 2–10 months (40%; with just 1 or 2 doses following vaccination schedule).

Table 2
The most prevalent serotypes to cause invasive pneumococcal disease in the pediatric and adult populations by age group during 2023 in Spain.

< 2		2-4		5-17		18-64		65-79		≥ 80	
Serotype	Case count (%)	serotype	Case count (%)	serotype	Case count (%)	serotype	Case count (%)	serotype	Case count (%)	serotype	Case count (%)
24F	26 (15.29)	3	23 (22.33)	8	25 (25.51)	8	402 (31.04)	3	196 (21.59)	3	129 (20.91)
3	24 (14.12)	24F	18 (17.48)	3	18 (18.37)	3	208 (16.06)	8	145 (15.97)	8	85 (13.78)
8	13 (7.65)	22F	9 (8.74)	22F	6 (6.12)	4	81 (6.25)	22F	73 (8.04)	22F	30 (4.86)
15B	12 (7.06)	19A	8 (7.77)	24F	5 (5.10)	22F	63 (4.86)	6C	38 (4.19)	9N	24 (3.89)
22F	11 (6.47)	15A	6 (5.83)	19A	5 (5.10)	9N	48 (3.71)	19A	33 (3.63)	19A	24 (3.89)
10A	11 (6.47)	23B	5 (4.85)	19F	4 (4.08)	12F	43 (3.32)	9N	30 (3.30)	11A	24 (3.89)
38	9 (5.29)	8	4 (3.88)	23A	4 (4.08)	10A	42 (3.24)	11A	28 (3.08)	23A	23 (3.73)
33F	8 (4.71)	19F	3 (2.91)	6C	3 (3.06)	19A	41 (3.17)	15A	28 (3.08)	15A	23 (3.73)
16F	6 (3.53)	9N	3 (2.91)	10A	3 (3.06)	19F	32 (2.47)	31	26 (2.86)	31	23 (3.73)
19A	6 (3.53)	15B	3 (2.91)	1	2 (2.04)	11A	30 (2.32)	38	26 (2.86)	6C	22 (3.57)
19F	5 (2.94)	23A	3 (2.91)	23B	2 (2.04)	23B	29 (2.24)	24F	26 (2.86)	24F	17 (2.76)
15A	5 (2.94)	38	2 (1.94)	38	2 (2.04)	15A	24 (1.85)	10A	24 (2.64)	33F	15 (2.43)
11A	4 (2.35)	1	2 (1.94)	11A	2 (2.04)	24F	21 (1.62)	23A	21 (2.31)	10A	14 (2.27)
15C	4 (2.35)	6C	2 (1.94)	12F	2 (2.04)	23A	20 (1.54)	23B	21 (2.31)	15B	14 (2.27)
35B	3 (1.76)	33F	2 (1.94)	9N	2 (2.04)	6C	19 (1.47)	15B	20 (2.20)	19F	13 (2.11)
4	3 (1.76)	35F	2 (1.94)	4	1 (1.02)	33F	19 (1.47)	33F	19 (2.09)	35F	12 (1.94)
35F	2 (1.18)	11A	2 (1.94)	14	1 (1.02)	35B	16 (1.24)	16F	16 (1.76)	38	11 (1.78)
12F	2 (1.18)	10A	2 (1.94)	7C	1 (1.02)	15B	16 (1.24)	4	15 (1.65)	16F	11 (1.78)
7B	2 (1.18)	9V	1 (0.97)	15B	1 (1.02)	31	15 (1.16)	35F	15 (1.65)	35B	10 (1.62)
31	2 (1.18)	16F	1 (0.97)	18C	1 (1.02)	20	13 (1.00)	19F	15 (1.65)	12F	10 (1.62)
Other	12 (7.06)	Other	2 (1.94)	Other	8 (8.16)	Other	113 (8.73)	Other	93 (10.24)	Other	83 (13.45)
Total	**170**	**Total**	**103**	**Total**	**98**	**Total**	**1295**	**Total**	**908**	**Total**	**617**

In adults aged ≥65 years old, we also found a dramatic reduction of 53% IPD cases in 2020 (1477 cases in 2019 vs 694 cases in 2020), followed by a lesser reduction of 34% in 2021 (458 cases) and a rise in 2022 (905 cases) and 2023 (1525) achieving pre-pandemic levels (Fig. 2B). The distribution of three most frequent serotypes was very similar in the evaluated period. During 2019–2023, serotypes 8 and 3 accounted for more than 30% of all IPD cases in adults. Serotype 8 was the most prevalent serotype during 2019–2021, but in 2022 and 2023, serotype 3 became the most common serotype causing IPD in adults aged ≥65 years old (Fig. 2B), which is consistent with the increase of serotype 3 in pediatric population in 2023 as the most frequent serotype (Fig. 2). Overall, our results show that COVID-19 pandemic had a clear impact on the burden of disease during the first two years reducing the global incidence of IPD with a modest impact in the serotype distribution as the most frequent serotypes remained constant.

To characterize the most current epidemiology of circulating serotypes causing IPD in different age groups, we evaluated in detail the year 2023 (Table 2). In children < 2 years old, serotypes 24F, 3, 8, 15B and 22F accounted for up to 51% of all IPD cases, whereas in children aged 2–4 years old, serotypes 3, 24F, 22F, 19A, and 15A were responsible for up to 62% of all cases (Table 2). It is also notable that most cases of serotype 8 in pediatric population are in older children (5–17 years old group) (Table 2). In young adults (18–64 years old group), just only two serotypes such as 8 and 3 were responsible for up to 47% of IPD cases and accounted for 38% and 35% of cases in adults aged ≥65 and ≥80 years old respectively (Table 2). Additionally, the relevance of serotype 4 in younger adults (18–64 years old) is worrisome because it is a vaccine-preventable serotype not present in children and older adults, and it is the third cause of IPD in young adults with 81 cases in 2023 vs 29 cases in 2019 (Table 2).

Contribution of different pneumococcal vaccines to prevent the burden of disease by circulating serotypes

In children, PCV15 would potentially avoid between 5–11% more IPD cases in comparison to PCV13. However, the use of PCV20 would prevent between 30–38% more IPD cases than PCV13 and PCV24 vaccine would protect at a similar level than PCV20 with 1–3% more cases than PCV20 (Fig. 3A). In adults ≥65 years old, with the last epidemiological year 2023, the use of PCV15 would increase the coverage up to 9% compared to PCV13 whereas the use of PCV20 or PPV23 would prevent up to 34% or 39% respectively in comparison to PCV13 (Fig. 3B). The use of future PCVs of broader spectrum would prevent up to 49% more cases for PCV21 and 39% for PCV24 when PCV13 was compared (Fig. 3B).

Discussion

Epidemiological surveillance of IPD is essential to evaluate the evolution of both vaccine and non-vaccine serotypes, thereby confirming the effectiveness of vaccination programs in the burden of disease. The detection of emerging serotypes not targeted by current vaccines is also another crucial aspect of surveillance programs that may guide the selection of serotypes for future vaccine formulations. Our study presents dynamic trends in IPD affecting various age groups in Spain from 2019–2023 covering the impact of COVID-19 pandemic. Previous studies worldwide have confirmed that the use of PCV13 in the pre-pandemic period was highly effective in preventing IPD in children, although there was some serotype replacement mainly by non-PCV13 serotypes, such as 24F and 8.[7,12–14]

The COVID-19 pandemic significantly reduced the burden of IPD across all age groups, particularly during 2020 and 2021, largely caused by the implementation of NPIs that contributed to a reduced transmission scenario. This pattern has been observed globally and extends to other invasive respiratory pathogens like *Neisseria meningitidis* and *Haemophilus influenzae* but not to non-respiratory bacterial species such as *Streptococcus agalactiae*.[11,15,16] Our data indicate that the resurgence of IPD cases started in 2021 for children and in 2022 for adults coinciding with the easing of pandemic restrictions, which is consistent with the situation in other countries.[11,17,18]

Regarding serotype distribution, during the COVID-19, the overall IPD decreased without significant changes in serotype dynamics during 2020–2021 in comparison to 2019. In children, serotype 24F was the leading cause of IPD until 2021 but dropped to second place in 2022 and 2023. The high prevalence of this serotype in the pediatric population is concerning because it is not covered by any of the licensed vaccines for the pediatric age group and it is associated with multidrug resistance and a high potential virulence including a special tropism for producing meningitis.[6,13,19,20] However, in 2022 and 2023, we have observed an important rise of serotype 3 in

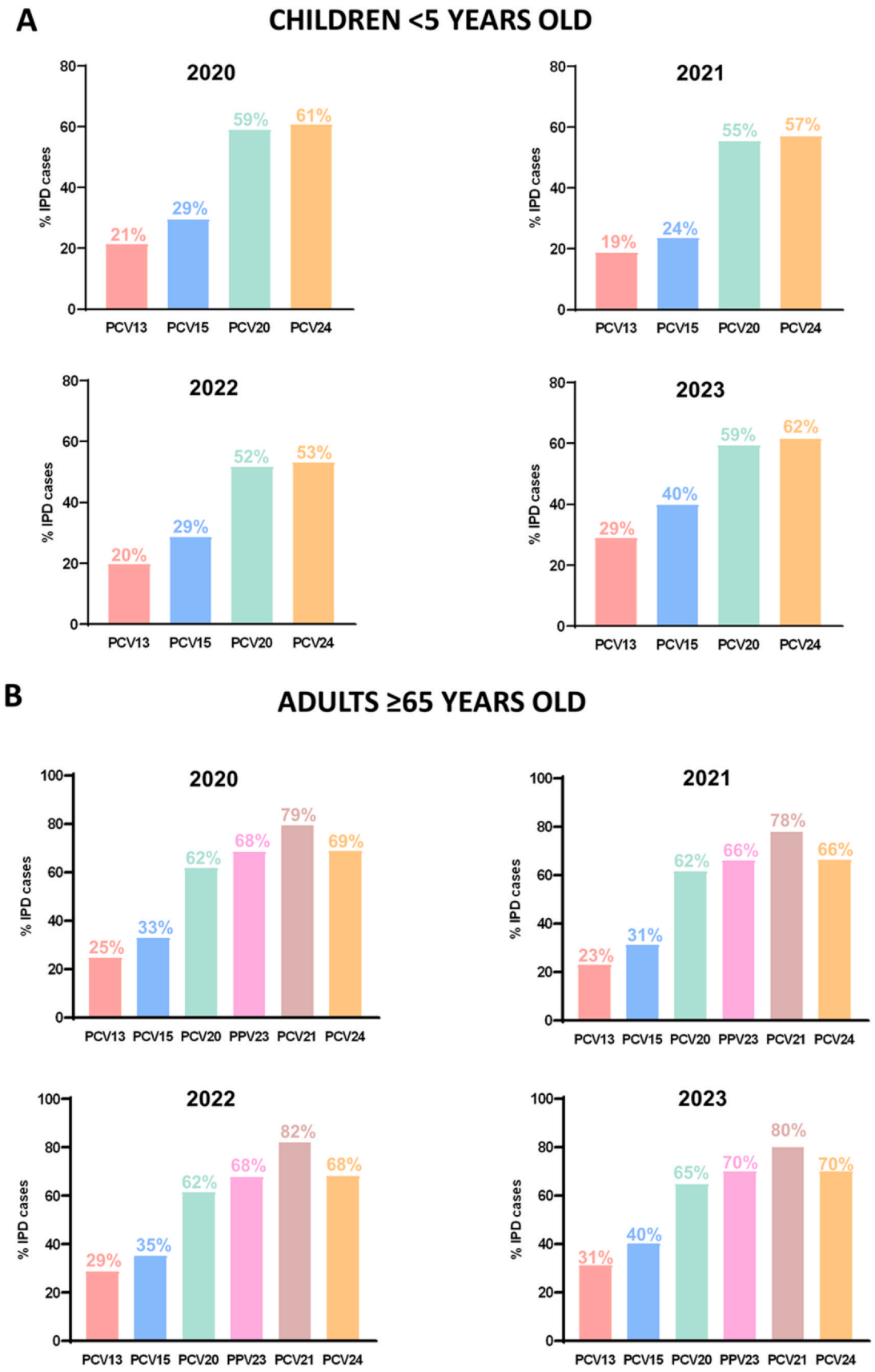


Fig. 3. Fraction of invasive pneumococcal disease that could be prevented by different PCVs and PPV23 during the period 2020–2023. Proportion of pneumococcal cases caused by serotypes included in PCV13 (red bars), PCV15 (blue bars), PCV20 (green bars), PCV24 (orange bars), PPV23 (pink bars), and PCV21 (brown bars) in children < 5 years old (A) or adults aged ≥65 years old (B).

children. This is surprising because this serotype is covered by PCV13, which is included in the Spanish national immunization schedule since 2016. Hence, the previously suggested weaker protection of PCV13 against this serotype and the short-lived trends in immunogenicity could explain its rise.[21]

In adults aged 65 years and older, serotypes 8 and 3 were the most prevalent between 2019 and 2021, accounting for more than 30% of all IPD cases. However, in 2022 and 2023, serotype 3 became the dominant serotype in adults aged 65 and above, as well as those 80 and older. A similar increase in serotype 3 has been recently published in the UK.[18] The lack of indirect protection from pediatric vaccination and the low immunogenicity with PCV13 and PPV23 against serotype 3 may explain its increased incidence in recent years.[7,21] The emergence of IPD cases by serotype 3 may be attributable to the global expansion of a particular lineage termed Clade II within CC180 serotype 3 population. This lineage differs from pre-vaccine pneumococcal strains in its non-capsular antigens, competence genes and even in the antibiotic susceptibility phenotype.[22] Another serotype showing an increasing trend in young adults (aged 18–64) is serotype 4. This is intriguing because this serotype is scarce in pediatric population, while in young adults was the third cause of IPD in 2023 and 2022 (81 and 35 cases, respectively) compared to 2019 when it was in 9th place (29 cases). A similar upsurge of serotype 4 has been noted in the U.S. among patients experiencing homelessness and drug abuse although in our study, the affected individuals did not suffer substantial health disparities.[23–25]

Clinical interventions involving antibiotic use during 2020 to prevent severe disease mediated by bacterial co-infections with SARS-CoV-2, have favored the emergence of multidrug resistance pneumococcal strains.[6] In this sense, the increased resistance to penicillin for non-vaccine serotype 11A during the COVID-19 pandemic is worrisome as it is the leading cause of multidrug-resistant IPD.[6,26] In Spain and other European countries, this multidrug resistance phenotype in serotype 11A pneumococci was associated with the spread of a vaccine scape through recombination of the worldwide disseminated PMEN3 clone (CC156-GPSC6), which invasive disease potential has been demonstrated.[27]

Prevention of IPD caused by vaccine serotypes requires a complex and multifactorial strategy. There are studies evaluating the use of 1 + 1 schedule showing comparable results to the 3 + 1 schedule, especially in regions with mature vaccination programs using PCVs or in combination with active catch-up campaigns.[18,28–30] The long-term use of available pneumococcal vaccines to elicit direct protection in vaccinated groups and the contribution of herd protection to non-vaccinated individuals is crucial. Achieving high vaccination coverage rates, especially among adults, is probably one of the most critical aspects. In this sense, new PCVs (PCV15 and PCV20) have been recently introduced in different pediatric and adult vaccination programs worldwide, and novel PCVs with broader spectrum (PCV21 and PCV24) are in different clinical trials, showing high immunogenic titers so far.[31,32] However, it is important to evaluate not only the number of additional serotypes that could be prevented with these new PCVs but also specific features of these vaccines should be considered. For instance, immunogenicity against serotype 3 is higher in PCV15 than in PCV13.[9,10] Vaccines with higher coverage such as PCV20 could prevent a higher proportion of IPD strains than PCV13 and PCV15 including up to 92% of non-susceptible strains to cefotaxime.[6] In our study, the vaccine with the highest coverage rate was PCV21, which has been developed specifically to prevent adult IPD and, thus, contains a different serotype distribution compared to other PCVs.[31] Additionally, PCV24 has the potential to induce direct protection by eliciting an immunogenic response against the corresponding CPS but also to the pneumococcal proteins that are present in many pneumococcal serotypes.[32] This is noteworthy because the use of pneumococcal conserved proteins as vaccine antigens could induce opsonophagocytic titers against numerous serotypes, and prevention of pneumonia and sepsis has been shown in preclinical studies.[33–36]

In summary, our study underscores the importance of continuous epidemiological surveillance of IPD, particularly in the context of evolving vaccination programs and public health crises like the COVID-19 pandemic. Our findings suggest that while existing vaccines have been effective in reducing IPD, the emergence of non-vaccine serotypes and multidrug-resistant strains warrants ongoing vigilance. The study also highlights the potential of newer vaccines with broader coverage, although their efficacy needs to be further validated. These insights are crucial for informing future vaccine policies and strategies for both children and adults.

Funding source

This work was supported by Ministerio de Ciencia e Innovación (MICINN) [grant PID2020-119298RB-I00] and internal funding from ISCIII. This study was also partially funded by grants from Merck Sharp Dohme [grant MISP#IISP60170], although this funder had no intervention in the results of this study.

Disclaimer

The findings and conclusions presented here are those of the authors and do not necessarily represent the official position of Instituto de Salud Carlos III (ISCIII).

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: JY has received grants from MSD-USA (MISP Call), Pfizer and MEIJI. JY has participated in advisory boards organized by GSK, MSD, and Pfizer. Jy declares payments of travel expenses and meeting fees from MSD and Pfizer. JS and SdM have participated in advisory boards organized by MSD. JLL reports congress registration fees and travel grants from GSK. Pfizer. MSD. Sanofi, Almirall, Ferrer. FMT declares that his institution received payment for conducting vaccine trials for Ablynx, Abbot, Seqirus, Sanofi, MSD, Merck, Pfizer, Roche, Regeneron, Janssen, Medimmune, Novavax, Novartis, and GSK; FMT also reports receiving honoraria for lectures from Sanofi, MSD, Moderna, GSK, Biofabri, AstraZeneca, Novavax, Janssen, and Pfizer. FMT declares payment of travel expenses and meeting fees from Pfizer, MSD, GSK, and Sanofi; and participation on data safety monitoring boards or advisory boards for Pfizer, ILiAD, Shionogi, GSK and Biofabri. FMT is also a member of WHO's European Technical Advisory Group of Experts, coordinator of the Spanish Pediatric Clinical Trials Network, and coordinator of WHO Collaborating Center for Vaccine Safety of Santiago de Compostela. JCS reports grants, congress registration fees, and travel grants from Pfizer and MSD. CA has received grants from MSD-USA (MISP Call), and Pfizer. CA has participated in advisory boards organized by MSD, and Pfizer. All other authors report no potential conflicts.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jinf.2024.106204.

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