Epidemiology of invasive pneumococcal disease in Catalonia. Report 2019-2020

Microbiological Reporting System of Catalonia (SNMC)

Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response

December 2022

Generalitat de Catalunya
Departament de Salut

Coordinated by:

Pilar Ciruela and Sonia Broner

Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.

Authors:

Pilar Ciruela,[1] Sonia Broner,[1] Conchita Izquierdo,[1] Xavier Ayneto,[1] Lorena Coronas,[1] Carme Muñoz-Almagro,[2,3] Román Pallarés,[4,5] Carmen Ardanuy,[5] Montse Martínez,[6] Carmen Cabezas,[7] Jacobo Mendioroz,[1] Catalan Working Group on Invasive Pneumococcal Disease.[8]

[1] Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.

[2] Hospital Universitari Sant Joan de Déu, Barcelona. Public Health Support Laboratory.

[3] Faculty of Medicine, International University of Catalonia, Barcelona.

[4] Hospital Universitari de Bellvitge, Barcelona.

[5] Faculty of Medicine, University of Barcelona.

[6] Preventive Medicine Service. Public Health Agency of Catalonia.

[7] Secretariat for Public Health. Public Health Agency of Catalonia.

[8] Catalan Working Group on Invasive Pneumococcal Disease: C. Esteva, M. F. de Sevilla, D. Henares (Hospital Universitari Sant Joan de Déu, Esplugues de Llobregat, Public Health Support Laboratory); I. Grau, J Càmara (Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat); F. Marco, C Pitart, M Fernández-Pittol (Hospital Clínic de Barcelona); A. Rivera, C. Berengua (Hospital de la Santa Creu i Sant Pau, Barcelona); A. González-Cuevas (Hospital General Parc Sanitari Sant Joan de Déu, Sant Boi de Llobregat); A. Díaz-Conradi (Hospital HM Infants, Barcelona); N. Larrosa, B. Viñado (Hospital Universitari Vall d'Hebron, Barcelona); J. Llaberia (SCIAS Hospital de Barcelona, Barcelona); M. Curriu (Hospital Sant Bernabé, Berga); C. Gallés, E. Capdevila, P. Hernández (Corporació de Salut del Maresme i la Selva, Calella); P. Gassiot, C. Mora (Hospital de Figueres, Figueres); J.M. Ramirez (Hospital Universitari Doctor Josep Trueta, Girona); C. Martí (Hospital General de Granollers, Granollers); G. Trujillo, J Lopez (Hospital Sant Joan de Déu, Fundació ALTHAIA, Manresa); G. Sauca, I. Valle (Hospital de Mataró, Mataró); E. Sanfeliu (Hospital d'Olot i Comarcal de la Garrotxa, Olot); F. Ballester, I. Pujol (Hospital Universitari Sant Joan de Reus, Reus); M. Olsina (Hospital General de Catalunya, Sant Cugat del Vallès); X. Raga (Hospital Sant Pau i Santa Tecla, Tarragona); F. Gómez-Bertomeu (Hospital Joan XXIII, Tarragona); M. O. Pérez-Moreno (Hospital Verge de la Cinta, Tortosa); A. Vilamala, M. Navarro (Hospital Universitari de Vic); M. Garcia, A. Bellés (Hospital Universitari Arnau de Vilanova de Lleida, Lleida); E. Padilla, N. Prim (Laboratori de Referència Catalunya, El Prat de Llobregat); A. Casabella, I. Sanfeliu, M. Alguacil (Parc Taulí Hospital Universitari, Institut d'Investigació i Innovació Parc Taulí I3PT, UAB, Sabadell); M. A. Benítez, E. Jou, C. Sanjosé (CLILAB Diagnòstics, Vilafranca del Penedès); M. Giménez, M. D. Quesada (Hospital Universitari Germans Trias i Pujol, Badalona); J. C. de la Fuente (Hospital Comarcal Móra d'Ebre, Móra d'Ebre); A. Calderón (Hospital Municipal de Badalona, Badalona); P. J. Ayala (Clínica Terres de l'Ebre, Tortosa); I. Suárez (Hospital Universitari Dexeus, Grupo Quirón Salud, Barcelona); J. Pérez-Jové (Catlab, Centre Analítiques Terrassa, AIE, Terrassa); M. Armas (Laboratori d'Anàlisis Dr. F. Echevarne, Barcelona); M. T. Bastida, R. Santos (Fundació Hospital Esperit Sant, Santa Coloma de Gramenet), O. González-Moreno (SYNLAB Diagnósticos Globales S.A.U., Esplugues de Llobregat); A. Oteiza, N. Torrellas, N. Claver (Hospital de Palamós, Palamós).

Acknowledgements

To the professionals who are part of the SNMC: Maria Mercè Nogueras and Aurora Sabrià.

To the European *Streptococcus pneumoniae* Invasive Disease network (SpIDnet).

To the Barcino working group.

Promoting Unit:

Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.

3rd edition:

Barcelona, November 2022

Language consultancy:

Language Planning Service, Ministry of Health

Accessible template design 1.06.
Communications Office. Corporate Identity

Table of contents

1 Introduction

Invasive pneumococcal disease (IPD) is a major public health problem worldwide with a high morbidity rate and the cause of a broad spectrum of diseases of varying severity, ranging from otitis media to pneumonia and meningitis. IPD is defined as a disease that is accompanied by the isolation or detection of DNA or antigen of *Streptococcus pneumoniae* from a normally sterile site (blood, cerebrospinal fluid, pleural fluid, peritoneal fluid, synovial fluid, etc.).

Over 100 *S. pneumoniae* serotypes have been identified based on the composition of the polysaccharide capsule. The circulation of these serotypes, and thus the epidemiology of IPD, have changed in recent years in parallel with the introduction of the pneumococcal conjugate vaccine.

Since 1993, surveillance of confirmed cases of IPD has been carried out through the Microbiological Reporting System of Catalonia (SNMC), which is coordinated by the Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response (SGVRESP). The SNMC is a basic health information system that forms part of the Epidemiological Surveillance Network of Catalonia and is made up of the 33 microbiology laboratories with their referral areas in hospital and out-of-hospital health centres (Annex 1).

These centres (55 public hospitals and 3 private hospitals) represent 92.3% of the acute care beds in public hospitals in the Integrated Public Health System of Catalonia (SISCAT).

Decree 203/2015,[3] of 15 September, creating the Epidemiological Surveillance Network of Catalonia and regulating reporting systems for notifiable diseases and epidemic outbreaks, establishes SNMC as one of the systems for reporting notifiable diseases. The Decree also creates a list of new notifiable diseases, which includes IPD as a notifiable disease exclusively by microbiological reporting.

Since 2012, the Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response (SGVRESP) of the Public Health Agency of Catalonia (ASPCAT) has participated in a European IPD "SpID-NET" active surveillance project (PROC/2012/031) "Assessing the impact of vaccination with conjugate vaccines on the epidemiology of the invasive pneumococcal disease in Europe", together with nine other European regions. The aim of the project is to carry out homogeneous active surveillance of IPD in Europe to increase knowledge of IPD epidemiology and analyse the overall impact and effectiveness of conjugate vaccines in infants under 5 years of age. The laboratory of the Hospital Sant Joan de Déu participates in this project as a public health support laboratory for IPD molecular surveillance.

From 2015 to 2019, the European IPD active surveillance project (PROC/2015/020) "SpID-NET" was extended to analyse the overall impact, mortality and effectiveness of pneumococcal conjugate vaccines in children under

5 years and adults aged 65 years and older. During this period, the monitoring network was extended to other European countries with a total of fifteen regions in eleven countries.[4]

The SGVRESP also participated in the "Pneumococcal Serotype Replacement and Distribution Estimation (PSERENADE)" project, funded by the Bill & Melinda Gates Foundation and the World Health Organization (WHO), together with 75 other countries around the world. The aim of this project was to measure the overall impact of conjugate vaccines on the incidence of IPD and pneumococcal meningitis in children and adults and to detect the distribution of serotypes during the pneumococcal conjugate vaccine era: Pn10 and Pn13.[11]

2 Objectives

The aim of this report is to describe the clinical and epidemiological characteristics and the distribution of IPD serotypes in different age groups during years 2019-2020 and to analyse the impact of the inclusion of the Pn13 vaccine in the routine schedule in 2016 on the incidence of IPD during years 2017-2020.

3 Methods

The information in this report is based on the notifications of confirmed acute cases of IPD issued by the laboratories that participated in the SNMC during years 2016-2020. A case of IPD is defined as a patient presenting symptoms suggestive of infection with isolation, DNA or antigen detection of *S. pneumoniae* from a normally sterile site.

During this period, in the context of the European IPD surveillance project (SpIDnet), the SGVRESP carried out enhanced and proactive surveillance of microbiological and clinical variables through various sources of information. Furthermore, since 2011, the Public Health Support Laboratory for IPD surveillance at Hospital Universitari Sant Joan de Déu has been responsible for identifying the *S. pneumoniae* serotype using the PCR technique and multilocus sequence typing (MLST) with samples received from certain laboratories. These samples are sent to the National Reference Laboratory for Pneumococci at the National Microbiology Centre in Majadahonda to identify the serotype of *S. pneumoniae*, using the Quellung reaction, and the antibiotic sensitivity of all samples received.

Serotype identification was carried out using the Quellung reaction and, when not possible, by PCR.

Socio-demographic and clinical data were sex and age (age groups < 5 years, 5-19 years, 20-64 years and 65 years and over), date of diagnosis, clinical presentation, personal or pathological history and evolution.

The personal or pathological history was divided into two mutually exclusive categories following the recommendations of the Advisory Committee on Immunization Practices (ACIP)[15]: (1) immunodeficient or high-risk, including chronic kidney failure, HIV, immunodeficiency (medically induced or innate), asplenia, haematological or metastatic disease, CSF fistula and previous neurosurgery, and (2) immunocompetent or at-risk, including *diabetes mellitus*, congestive heart failure, chronic lung disease, cirrhosis, smoking and alcoholism. The presence of two or more comorbidities was classified as "> 1 high-risk condition" if one of these antecedents was high risk, and as "> 1 risk condition" otherwise.

The type of vaccine (Pn13/Pn23) and the number of doses received were also recorded. Laboratory information included the diagnostic technique (culture, PCR or antigen detection), antibiotic susceptibility and serotype, which was analysed taking into account whether it was included in the Pn13 conjugate vaccine, in the Pn23 vaccine and in the 3rd generation pneumococcal conjugate vaccines (Pn15 and Pn20).[16]

Determination of antibiotic sensitivity was performed for the antibiotics: penicillin, cefotaxime, erythromycin and levofloxacin. For the study of resistance, the cut-off points recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST)[17] were used, with the consensus of the SNMC Working Group according to the *Protocol for surveillance of antimicrobial resistance in Catalonia*.[18] The association of resistance to two or more antibiotics was analysed in accordance with their efficiency in the treatment of IPD.

With regard to statistical analyses, incidence rates were calculated based on demographic data from the Statistical Institute of Catalonia (Idescat) for the age groups analysed.

The impact analysis was performed using relative risk (RR) with 95% confidence intervals, assuming a Poisson distribution and comparing each year of the period 2017-2020 with 2016, using the formula (1-RR)*100. Year 2016 was considered the baseline, as it is the first year in which the Pn13 vaccine was routinely administered to children.

The Pn13 vaccine coverage for years between 2017 and 2020, with a universal immunisation schedule in children under 2 years of age with a full vaccination schedule, was between 81.8% and 91.0%,[19] respectively, while the estimated coverage of the Pn23 vaccine in adults aged 65-79 years was 63.1% and, in ≥80 years, 81.2% in 2017.[20]

The analysis was performed using the Statistical Package for Social Sciences (SPSS 27.0) and R 4.0.1 (R Development Core Team 2020).

4 Results

4.1 Incidence by age group and sex

During 2019 and 2020, 1,168 and 548 cases of IPD were reported, respectively, representing incidence rates of 15.2 and 7.0 cases per 100,000 inhabitants. The highest incidences in 2019 and 2020 occurred in adults aged 65 and over (41.2 and 17.3 cases per 100,000 inhabitants, respectively) (figure 1). The number of men was higher than that of women, with an incidence of 13.2 cases per 100,000 person-years and 9.0 cases per 100,000 person-years, respectively. The male:female ratio was 1.4 in 2019 and 1.5 in 2020.

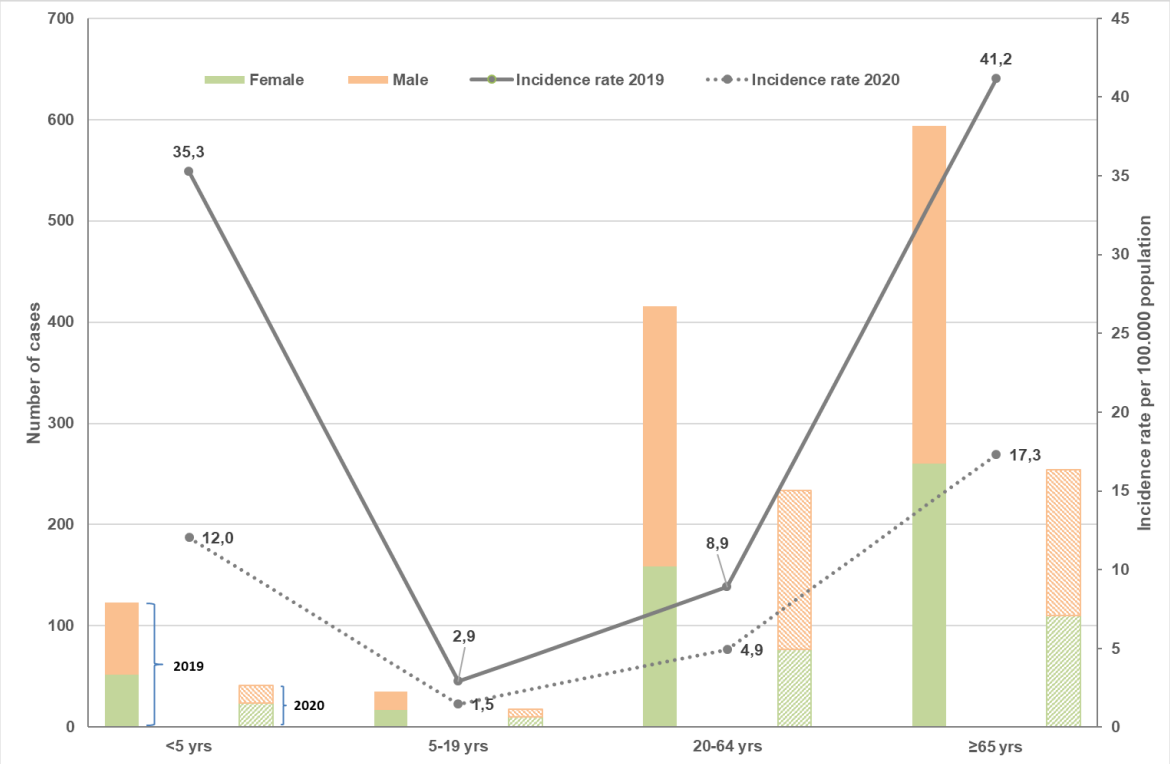
In the study period, diagnosis was performed by culture in 1,622 cases (94.5%); by PCR in 80 cases (4.7%) and by antigen detection in 14 cases (0.8%).

4.2 Impact of the 13-valent pneumococcal conjugate vaccine on the incidence of invasive pneumococcal disease

Between 2017 and 2019, a 10-15% increase in the overall incidence rate was observed compared to 2016 (table 1). The increase in incidence was significant in the 20-64 age group (between 18% and 25%) and in the 65 and over age group (18%) only in 2018 and 2019.

By contrast, 2020 showed a decrease in the incidence rate in all age groups compared to 2016 (between 31% and 57%) and also compared to 2019 (between 49% and 56%).

Figure 1. Incidence of invasive pneumococcal disease by age group and sex. Catalonia, 2019-2020



Source: Microbiological Reporting System of Catalonia. Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.

Table 1. Incidence of invasive pneumococcal disease by age group and year. Catalonia, 2016-2020

Age group	2016 No.	2016 Rate*	2017 No.	2017 Rate*	2018 No.	2018 Rate*	2019 No.	2019 Rate*	2020 No.	2020 Rate*
<5 yrs.	103	27.7	93	25.7	103	29.1	123	35.3	41	12.0
5-19 yrs.	37	3.2	31	2.6	28	2.3	35	2.9	18	1.5
20-64 yrs.	329	7.1	391	8.5	391	8.4	416	8.9	234	4.9
≥65 yrs.	448	32.5	496	35.4	534	37.6	594	41.2	254	17.3
Total	917	12.2	1,011	13.4	1,056	13.9	1,168	15.2	548[a]	7.0

Source: Microbiological Reporting System of Catalonia. Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.

No.: number of cases.

* Rate per 100,000 person-year.

[a] In 1 case the age was unknown.

Table 1. (Continued)

Age group	2017 vs. 2016 RR** (IC 95%)	2018 vs. 2016 RR** (IC 95%)	2019 vs. 2016 RR** (IC 95%)	2020 vs. 2016 RR** (IC 95%)
<5 yrs.	0.92 (0.69-1.24)	1.05 (0.79-1.39)	1.27 (0.97-1.67)	0.43 (0.29-0.63)
5-19 yrs.	0.83 (0.50-1.37)	0.74 (0.43-1.24)	0.91 (0.56-1.48)	0.46 (0.25-0.83)
20-64 yrs.	1.19 (1.02-1.38)	1.18 (1.02-1.37)	1.25 (1.08-1.45)	0.69 (0.58-0.82)
≥65 yrs.	1.09 (0.96-1.24)	1.16 (1.02-1.31)	1.27 (1.12-1.44)	0.53 (0.45-0.62)
Total	1.10 (1.00-1.20)	1.14 (1.04-1.25)	1.25 (1.14-1.36)	0.58 (0.52-0.64)

Source: Microbiological Reporting System of Catalonia. Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.
No.: number of cases.
* Rate per 100,000 person-year.
** RR: relative risk.

4.3 Clinical signs

During 2019 and 2020, the majority of cases presented pneumonia with percentages of 79.2% (925/1,168) and 75.5% (414/548), respectively. Meningitis accounted for 8.0% (94 cases) in 2019 and 9.9% (54 cases) in 2020. Similar percentages (8.3% and 8.2%) were observed for occult bacteraemia in the two years, with other clinical manifestations accounting for 4.5% and 6.4%, respectively (table 2).

Pneumonia was the most frequent clinical presentation in all age groups. The incidence rate was higher in adults aged 65 years and over with values of 34.6 and 17.3 cases per 100,000 inhabitants in 2019 and 2020, respectively. Meningitis showed higher incidence rates in children under 5 years of age (4.3 and 1.8 cases per 100,000 inhabitants, respectively).

Table 2. Incidence of invasive pneumococcal disease according to clinical manifestations and age groups. Catalonia, 2019-2020

Year and clinical entity	<5 yrs. No.	<5 yrs. Rate*	5-19 yrs. No.	5-19 yrs. Rate*	20-64 yrs. No.	20-64 yrs. Rate*	≥65 yrs. No.	≥65 yrs. Rate*	Total No.	Total Rate*
2019										
Pneumonia	70	20.1	17	1.4	339	7.1	499	34.6	925	12.0
Meningitis	34	9.7	7	0.6	25	0.5	31	2.1	97	1.2
Occult bacteraemia	15	4.3	10	0.8	34	0.7	35	2.4	94	1.2
Other[a]	4	1.1	1	0.1	18	0.4	29	2.0	52	0.6
Total	123	35.3	35	2.9	416	8.8	594	41.2	1168	15.2
2020										
Pneumonia	29	8.5	14	1.1	181	3.8	190	12.9	414	5.3
Meningitis	5	1.5	2	0.2	18	0.4	20	1.4	45	0.5
Occult bacteraemia	6	1.8	1	0.1	23	0.5	24	1.6	54	0.6
Other[b]	1	0.3	1	0.1	12	0.3	20	1.4	35	0.4
Total	41	12.0	18	1.5	234	4.9	254	17.3	548[1]	7.0

Source: Microbiological Reporting System of Catalonia. Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.
No.: number of cases.
* Rate per 100,000 person-year.
[1] In one case age was unknown.
[a] Arthritis: 15; peritonitis/abdominal: 21; cellulite: 5; endocarditis: 3; other: 8.
[b] Arthritis: 7; peritonitis/abdominal: 23; other: 5.

4.4 Underlying medical conditions or personal history

66.4% (775/1,168) of cases with IPD in 2019 and 68.1% (373/548) in 2020 had an underlying medical condition (UMC). The 65 and over age group presented some UMC in 82% of cases in 2019 and 83% of cases in 2020.

During 2019 and 2020, the percentages of cases with immunosuppressive diseases were 50.2% and 48.8%, respectively (table 3).

Table 3. Distribution of cases of invasive pneumococcal disease by type of underlying medical condition. Catalonia, 2019-2020

Underlying medical condition	2019 No. (%)	2020 No. (%)
Immunocompetence	386 (49.8)	191 (51.2)
Cardiovascular	60 (7.7)	23 (6.2)
Respiratory	22 (2.8)	16 (4.3)
Diabetes	39 (5)	25 (6.7)
Alcohol	12 (1.5)	4 (1.1)
Cirrhosis	1 (0.1)	4 (1.1)
Smoking	68 (8.8)	38 (10.2)
Other risk factors	0 (0)	2[a] (0.5)
More than one risk factors	184 (23.7)	79 (21.2)
Immunosuppression	389 (50.2)	182 (48.8)
Kidney	23 (3)	11 (2.9)
Immunodeficiency*	80 (10.3)	42 (11.3)
Asplenia	0 (0)	0 (0)
Other high-risk factors	1[b] (0.1)	1[c] (0.3)
More than one high-risk factor	284 (36.6)	126 (33.8)
Total number of cases	775 (100)	373 (100)

Source: Microbiological Reporting System of Catalonia. Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.
No.: number of cases.
* Leukaemia, lymphoma, multiple myeloma, Hodgkin's disease, other neoplasms, solid organ or haematopoietic progenitor transplantation, immunosuppressive therapy, HIV infection
[a]: CSF fistula
[b]: Kidney and liver transplantation
[c]: Lung transplantation

4.5 Clinical course of IPD

In 2019, cases requiring hospital admission accounted for 89.0% (1,039/1,168) of all reported cases and of these, 17.6% (183/1,039) were admitted to the intensive care unit (ICU). During 2020, the percentage of inpatients was 88.5% (485/548)

and 20.8% (101/485) of those were admitted to the ICU (table 4). No significant differences were observed between the two years in the percentage of cases hospitalised and those admitted to the ICU.

In 2019 and 2020, 148 and 68 deaths were recorded, resulting in case fatality rates of 13.0% and 12.6%, respectively, with no significant differences between these years. Case fatality is highest in the 65+ age group and no deaths were recorded in the < 20 age group (table 5).

85.8% of the cases that died in 2019 presented some UMC, and 86.8% in 2020.

Table 4. Distribution by age group of cases hospitalised and admitted to the ICU for invasive pneumococcal disease. Catalonia, 2019-2020

Age group	2019 Hospitalised No. (%)	2019 Admitted to an ICU No. (%)	2020 Hospitalised No. (%)	2020 Admitted to an ICU No. (%)
<5 yrs.	105 (85.4)	23 (21.9)	33 (80.5)	6 (18.2)
5-19 yrs.	33 (94.3)	10 (30.3)	14 (77.8)	3 (21.4)
20-64 yrs.	353 (84.9)	92 (26.1)	204 (87.2)	54 (26.5)
≥65 yrs.	548 (92.3)	58 (10.6)	234 (92.1)	38 (16.2)
Total	1,039 (89.0)	183 (17.6)	485 (88.5)	101 (20.8)

Source: Microbiological Reporting System of Catalonia. Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.
No.: number of cases.

Table 5. Invasive pneumococcal disease case fatality by age. Catalonia, 2019-2020

Age group	2019 Death No.	2019 Fatality %	2020 Death No.	2020 Fatality %
<5 yrs.	0	0	0	0
5-19 yrs.	0	0	0	0
20-64 yrs.	29	7.2	17	7.4
≥65 yrs.	119	20.4	51	20.3
Total	148	13.0	68	12.6

Source: Microbiological Reporting System of Catalonia. Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.
No.: number of cases.

4.6 Serotype survey by age group

The serotype was identified in 87.1% of the diagnosed cases in 2019 and 80.5% in 2020, and 43 and 37 different serotypes were detected, respectively. The most frequent serotypes were 8 and 3, accounting for 31.9% of all cases in 2019 and 31.3% of cases in 2020.

In children under 5 years of age, the most frequent serotypes were 3 (16.5%), 24F (13.6%) and 12F (10.7%) in 2019. As included in the Pn13, Pn15 and Pn20 conjugate vaccines, they accounted for 31.1%, 35.0% and 56.3%, respectively. During 2020, the most frequent serotypes were 3 (22.9%), 23B (14.3%) and 24F (11.4%) (figure 2) and serotypes included in the Pn13, Pn15 and Pn20 vaccines accounted for 25.7%, 31.4% and 48.6%, respectively.

In 2019, in the 5-19 age group, serotypes 3 (25.9%) and 8 (14.7%) were the most frequent, and the serotypes included in the Pn13 and Pn15 vaccines accounted for 51.9%, and in Pn20, 77.8%. In 2020, the most frequent serotypes were 8 (33.3%) and 3 (26.7%), and serotypes included in the Pn13 and Pn15 vaccines accounted for 33.3%, and those included in the Pn20 vaccine, for 73.3%.

During 2019, in cases aged 20-64 years the most frequent serotypes were 8 (27.1%), 3 (12.2%) and 12F (10.3%), and serotypes included in the Pn13, Pn15 and Pn20 vaccines accounted for 30.2%, 36.4% and 79.6%, respectively. In 2020, the most frequent serotypes were 8 (28.3%), 3 (11.1%) and 9N (5.6%), and the percentages of serotypes included in the Pn13, Pn15 and Pn20 vaccines were 30.2%, 35.8% and 75.4%, respectively.

The most frequent serotypes in adults aged 65 years and over during 2019 were 8 (15.6%) and 3 (11.6%), while serotypes included in the Pn13, Pn15 and Pn20 vaccines accounted for 26.5%, 35.2% and 64.8%, respectively, and those included in the Pn23 vaccine accounted for 70.4%. In 2020, the most frequent serotypes were 8 (13.2%) and 3 (11.8%), and serotypes included in the Pn13, Pn15 and Pn20 vaccines accounted for 23.8%, 31.0% and 52.9%, respectively, and serotypes included in the Pn23 vaccine accounted for 61.9%.

4.7 Impact of the 13-valent pneumococcal conjugate vaccine on the incidence and distribution of serotypes by age group

No statistically significant changes in the incidence of IPD in children under 5 years of age were observed when comparing years 2017-2019 with 2016, either overall or in the serotype groups included and not included in the Pn13 vaccine. This was mainly due to the persistence of serotype 3 (included in Pn13) and serotype 24F (not included in Pn13).

On the other hand, in 2020, coinciding with the COVID-19 pandemic, a decrease in the incidence of 67% of the serotypes included in the Pn13 vaccine and 46% of those not included (non-Pn13) was observed, possibly due to measures taken during lockdown and other non-drug measures put in place to reduce SARS-CoV-2 transmission (table 6).

As for the 5-19 age group, the incidence of serotypes included in the Pn13 vaccine remained stable in years 2017 and 2019, while in the years 2018 and 2020,

decreases of 63% and 77% were observed in the incidence of serotypes included in the Pn13 vaccine.

With regard to the 20-64 age group, in 2017 and 2019 the incidence of serotypes included in the Pn13 vaccine increased by 40% and 39%, respectively, although the non-Pn13 also increased in 2019 (27%). By contrast, a decrease in the incidence was observed in 2020 for the same serotype groups (34%-39%).

In the 65 and over age group, however, increases of 19% and 41% were observed in the incidence of non-Pn13 serotypes in 2018 and 2019, respectively. In 2020, there were decreases of 54% and 40% in the incidence of the Pn13 and non-Pn13 serotypes.

In the data presented above, it is important to consider that the extraordinary measures taken during the COVID-19 pandemic in 2020 may have contributed significantly to the reduction of IPD incidence overall and across all age groups and serotype groups and thus evidenced a change in the epidemiology of the disease. In this regard, in a study carried out with three paediatric hospitals in Barcelona, a reduction in IPD in 2020 compared to 2018-2019 was observed, which was more significant in the second quarter of 2020, during lockdown.[21]

Table 6. Distribution of serotypes causing invasive pneumococcal disease by age group and year. Catalonia, 2016-2020

Age group	2016 No.	2016 Rate*	2017 No.	2017 Rate*	2018 No.	2018 Rate*	2019 No.	2019 Rate*	2020 No.	2020 Rate*
<5 yrs.	83	22.4	81	22.3	90	25.4	103	29.5	35	10.3
Pn13	30	8.1	27	7.4	24	6.8	32	9.2	9	2.6
non-Pn13	53	14.3	54	14.9	66	18.6	71	20.3	26	7.6
Pn15	36	9.7	31	8.6	27	7.6	36	10.3	11	3.2
Pn20	46	12.4	51	14.1	43	12.1	57	16.3	17	5.0
Pn23	47	12.7	53	14.6	45	12.7	58	16.6	17	5.0
5-19 yrs.	31	0.3	25	2.1	23	1.9	27	2.2	15	1.2
Pn13	21	0.2	13	1.1	8	0.7	14	1.2	5	0.4
non-Pn13	10	0.1	12	1.0	15	1.3	13	1.1	10	0.8
Pn15	22	1.9	13	1.1	9	0.8	14	1.2	5	0.4
Pn20	27	2.3	20	1.7	17	1.4	21	1.7	11	0.9
Pn23	27	2.3	22	1.9	18	1.5	22	1.8	11	0.9
20-64 yrs.	278	6.0	333	7.2	326	7.0	368	7.9	178	3.8
Pn13	79	1.7	111	2.4	92	2.0	111	2.4	54	1.1
non-Pn13	199	4.3	222	4.8	234	5.1	257	5.5	124	2.6
Pn15	94	2.0	136	2.9	114	2.5	134	2.9	64	1.3
Pn20	207	4.5	248	5.4	242	5.2	293	6.3	135	2.8
Pn23	220	4.8	268	5.8	257	5.6	308	6.6	149	3.1
≥65 yrs.	373	27.0	433	30.9	440	31.0	517	35.8	210	14.3
Pn13	116	8.4	133	9.5	126	8.9	137	9.5	50	3.4
non-Pn13	257	18.6	300	21.4	314	22.1	380	26.3	160	10.9
Pn15	147	10.7	162	11.6	160	11.3	182	12.6	65	4.4
Pn20	239	17.3	276	19.7	263	18.5	335	23.2	111	7.6
Pn23	261	18.9	293	20.9	289	20.3	364	25.2	130	8.9
Total	765	10.2	872	11.5	879	11.6	1015	13.2	438	5.6
Pn13	246	3.3	284	3.8	250	3.3	294	3.8	118	1.5
non-Pn13	519	6.9	588	7.8	629	8.3	721	9.4	320	4.1
Pn15	299	4.0	342	4.5	310	4.1	366	4.8	145	1.9
Pn20	519	6.9	595	7.9	565	7.4	706	9.2	274	3.5
Pn23	555	7.4	636	8.4	609	8.0	752	9.8	307	3.9

Source: Microbiological Reporting System of Catalonia. Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.

*Rate per 100,000 person-year.

**RR: relative risk.

No.: number of cases; Pn13: serotypes included in the 13-valent pneumococcal conjugate vaccine, Pn15: serotypes included in the 15-valent pneumococcal conjugate vaccine, Pn20: serotypes included in the 20-valent pneumococcal conjugate vaccine, Pn23: serotypes included in the 23-valent pneumococcal polysaccharide vaccine.

Table 6. (Continued)

Age group	RR** 2017 vs. 2016	RR** 2018 vs. 2016	RR** 2019 vs. 2016	RR** 2020 vs. 2016
<5 yrs.	1.00 (0.73-1.37)	1.14 (0.83-1.55)	1.32 (0.98-1.78)	**0.46 (0.30-0.69)**
Pn13	0.92 (0.53-1.60)	0.84 (0.47-1.48)	1.14 (0.67-1.93)	**0.33 (0.14-0.71)**
non-Pn13	1.04 (0.70-1.55)	1.31 (0.90-1.91)	1.43 (0.98-2.07)	**0.54 (0.32-0.87)**
5-19 yrs.	0.80 (0.45-1.39)	0.72 (0.40-1.28)	0.84 (0.48-1.45)	**0.46 (0.23-0.87)**
Pn13	0.61 (0.28-1.28)	**0.37 (0.14-0.87)**	0.64 (0.30-1.32)	**0.23 (0.07-0.61)**
non-Pn13	1.18 (0.47-3.06)	1.46 (0.61-3.63)	1.25 (0.51-3.18)	0.95 (0.35-2.53)
20-64 yrs.	**1.20 (1.02-1.41)**	1.17 (0.99-1.38)	**1.31 (1.11-1.53)**	**0.62 (0.51-0.75)**
Pn13	**1.40 (1.04-1.90)**	1.16 (0.85-1.59)	**1.39 (1.03-1.87)**	**0.66 (0.46-0.95)**
non-Pn13	1.11 (0.92-1.36)	1.17 (0.97-1.42)	**1.27 (1.05-1.54)**	**0.61 (0.48-0.76)**
≥65 yrs.	1.14 (0.99-1.32)	1.15 (0.99-1.32)	**1.33 (1.16-1.52)**	**0.53 (0.44-0.63)**
Pn13	1.13 (0.87-1.46)	1.05 (0.81-1.37)	1.13 (0.88-1.46)	**0.41 (0.28-0.57)**
non-Pn13	1.15 (0.97-1.36)	**1.19 (1.00-1.40)**	**1.41 (1.20-1.66)**	**0.59 (0.48-0.72)**
Total	**1.14 (1.03-1.25)**	**1.14 (1.03-1.25)**	**1.30 (1.18-1.43)**	**0.55 (0.49-0.62)**
Pn13	1.15 (0.97-1.37)	1.01 (0.84-1.20)	1.17 (0.99-1.39)	**0.46 (0.37-0.58)**
non-Pn13	1.13 (1.00-1.27)	**1.20 (1.07-1.35)**	**1.36 (1.21-1.53)**	**0.60 (0.52-0.69)**

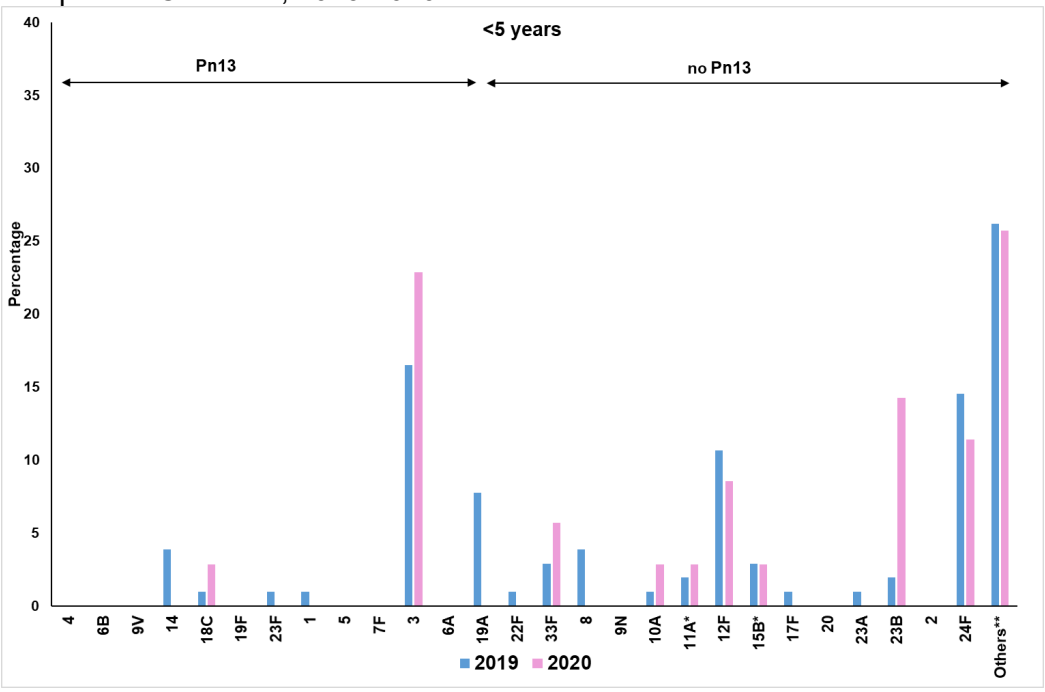
Source: Microbiological Reporting System of Catalonia. Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response Public Health Agency of Catalonia.

* Rate per 100,000 person-year.

** RR: relative risk.

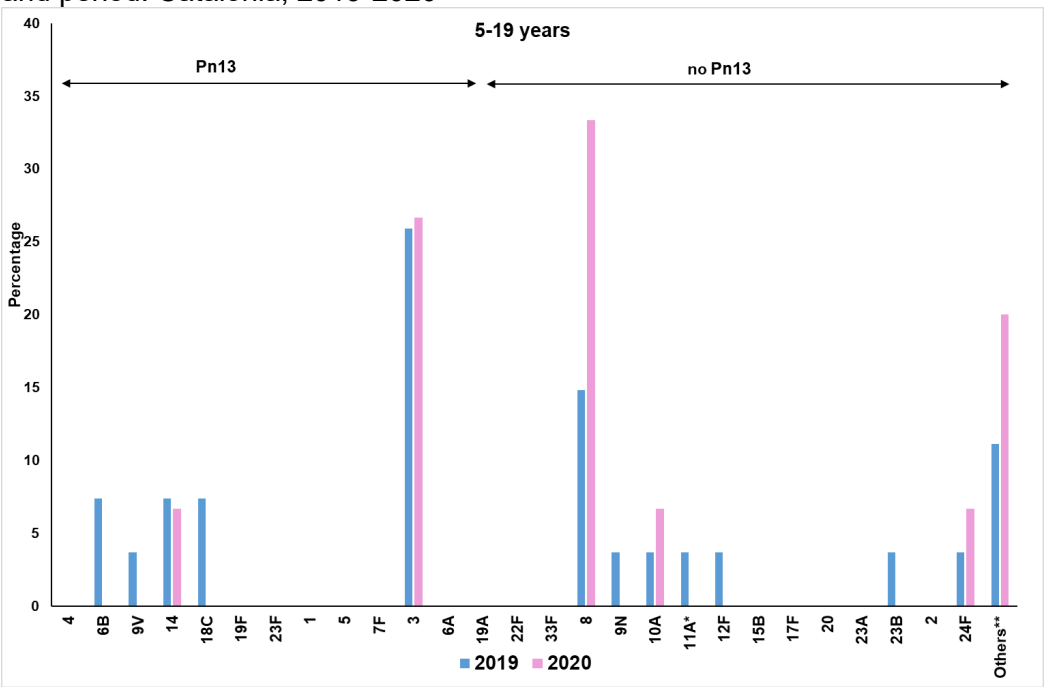
No.: number of cases; Pn13: serotypes included in the 13-valent pneumococcal conjugate vaccine.

Figure 2a. Distribution of serotypes causing invasive pneumococcal disease by age group and period. Catalonia, 2019-2020



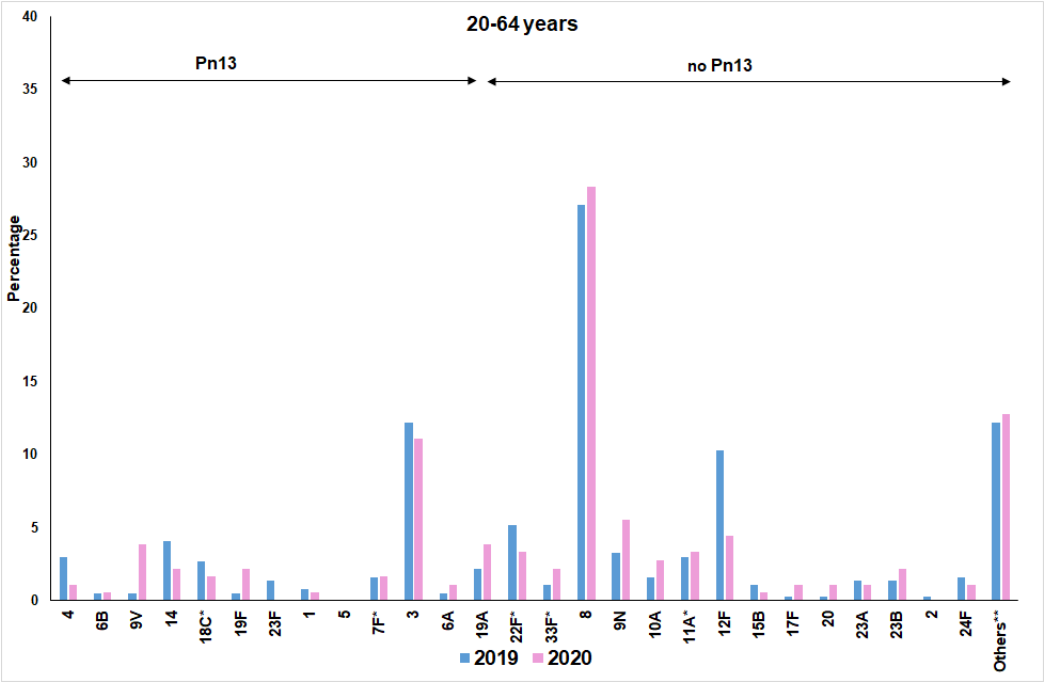
* In five cases the serotype was identified at group level only: two 11A/D, one 15B/C, one 24B/F and one 24F/A.
** 15A, 15C, 16F, 21, 35B, 38, 7B and other non-vaccine serotypes.

Figure 2b. Distribution of serotypes causing invasive pneumococcal disease by age group and period. Catalonia, 2019-2020



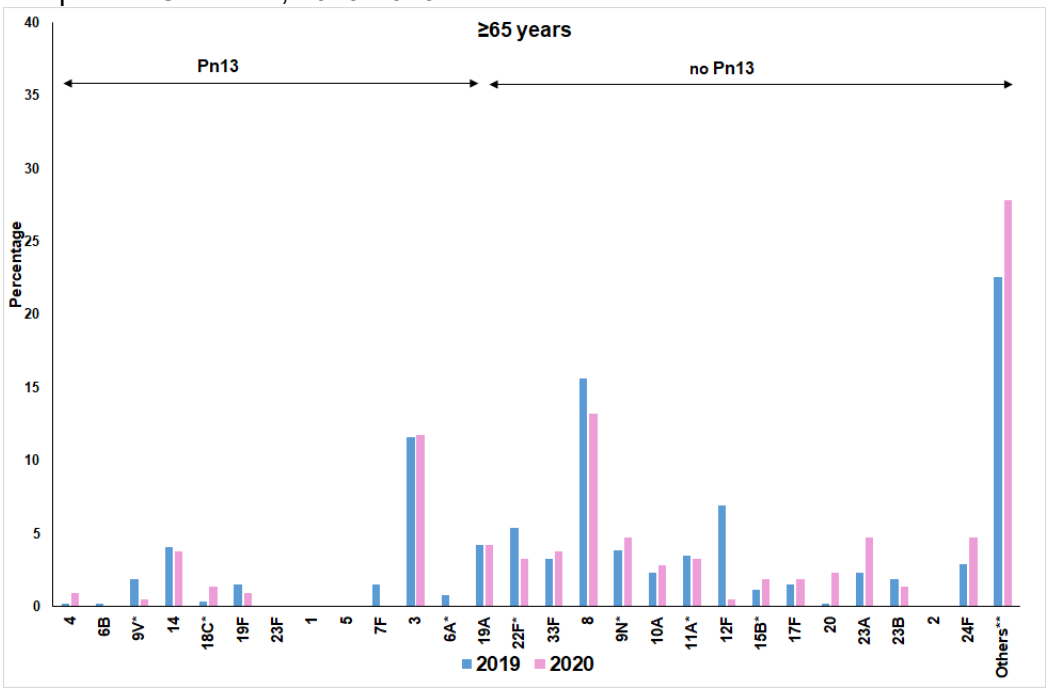
* In one case the serotype was identified at group level only: one 11A/D.
** 6C, 16F, 31, 35B, 35F and other non-vaccine serotypes.

Figure 2c. Distribution of serotypes causing invasive pneumococcal disease by age group and period. Catalonia, 2019-2020



* In five cases the serotype was identified at group level only: one 7F/A, two 11A/D, one 22F/A and one 33F/A.
** 15A, 16F, 21, 27, 28A, 29, 31, 35B, 35F, 38, 6C, 7B, 7C, 9L and other non-vaccine serotypes.

Figure 2d. Distribution of serotypes causing invasive pneumococcal disease by age group and period. Catalonia, 2019-2020



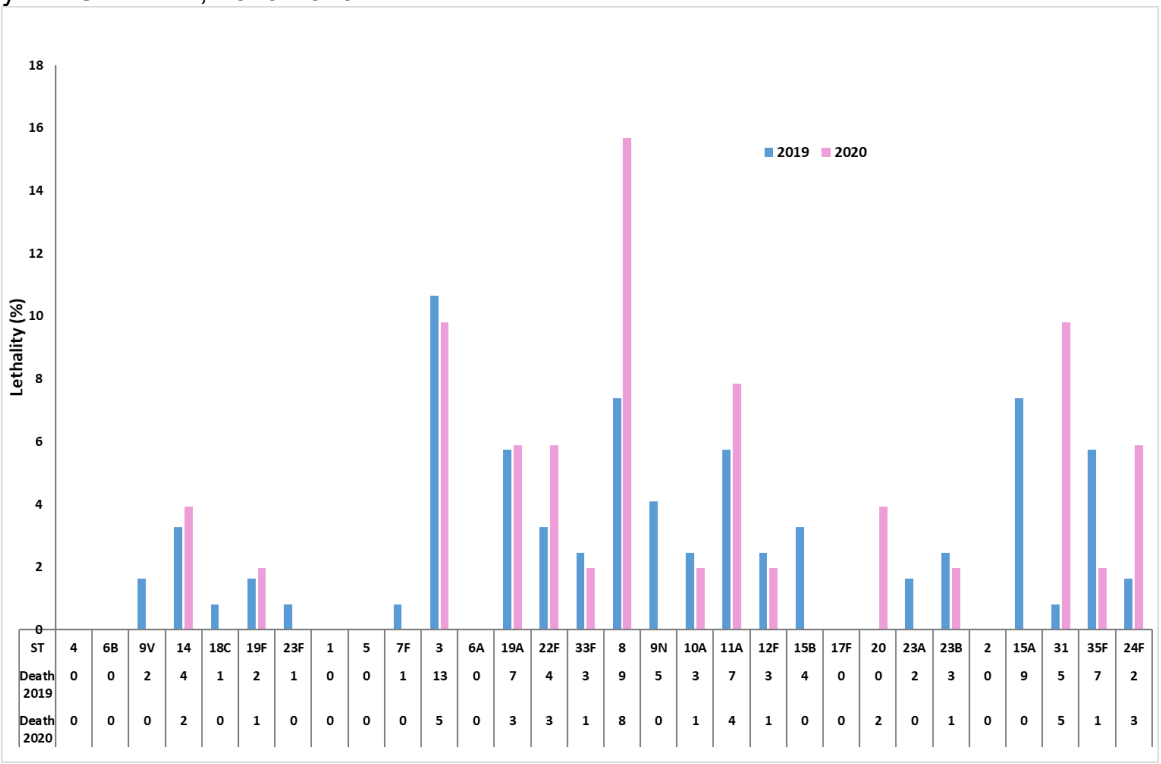
* In eight cases the serotype was identified at group level only: one 6A/C/D, two 9N/L, one 9V/L, three 11A/D and one 18B/C.

** 10B, 13, 15A, 15C, 16F, 21, 27, 28A, 29, 31, 34, 35B, 35F, 38, 6C, 7B, 7C, 9L and other non-vaccine serotypes.
Pn13: serotypes included in the 13-valent pneumococcal conjugate vaccine; non-Pn13: serotypes not included in the 13-valent pneumococcal conjugate vaccine.
Source: Microbiological Reporting System of Catalonia. Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.

4.8 Serotypes and fatality

Of the 148 deaths reported during 2019, the serotype was identified in 122 cases, with serotypes 3 (10.7%), 8 (7.4%) and 15A (7.4%) having the highest case fatality rates. In 2020, meanwhile, the serotype was identified in 50 of the 68 cases with deaths, and the most frequent serotypes were 8 (15.7%), 3 (9.8%) and 31 (9.8%) (figure 3).

Figure 3. Distribution of invasive pneumococcal disease case fatality by serotype and year. Catalonia, 2019-2020



ST	4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A	22F	33F	8	9N	10A	11A	12F	15B	17F	20	23A	23B	2	15A	31	35F	24F
Death 2019	0	0	2	4	1	2	1	0	0	1	13	0	7	4	3	9	5	3	7	3	4	0	0	2	3	0	9	5	7	2
Death 2020	0	0	0	2	0	1	0	0	0	0	5	0	3	3	1	8	0	1	4	1	0	0	2	0	1	0	0	5	1	3

Source: Microbiological Reporting System of Catalonia. Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.
ST: Serotype

4.9 Pneumococcal vaccination

The pneumococcal vaccines used in Catalonia are the polysaccharide vaccine Pn23, which was recommended in 1999, and the conjugate vaccines Pn13, which replaced Pn7 in 2010, and more recently, in October 2022, the Pn20 vaccine. The indications and serotypes included in each of the vaccines are listed in table 7.

Table 7. Characteristics of pneumococcal vaccines

Pneumococcal vaccine	Serotypes included	Year of introduction to Catalonia	Indication	Year of introduction to the calendar
Heptavalent conjugate (Pn7 vaccine)	4, 6B, 9V, 14, 18C, 19F and 23F	2001	<5 years with risk factors	No
Decavalent conjugate (Pn10 vaccine)	Pn7 plus serotypes 1, 5 and 7F	2009	<5 years with risk factors	No
Conjugate 13-valent (Pn13 vaccine)	Pn10 plus serotypes 3, 6A and 19A	2010	From 2010 to June 2016: <5 years with risk factors	July 2016: * ≤2 years * people with risk factors
Polysaccharide 23-valent (Pn23 vaccine)	Pn10 plus serotypes: 2, 3, 9N, 10A, 11A, 12F, 15B, 17F, 19A, 20, 22F and 33F	1999	From 1999 to June 2016: Recommended * ≥60 years * >2 years with risk factors	July 2016: ≥65 years
Conjugate 20-valent (Pn20 vaccine)	Pn13 plus serotypes 8, 10A, 11A, 12F, 15B, 22F and 33F	2022		October 2022: ≥65 years

4.9.1 Pneumococcal conjugate vaccine Pn13

During 2019 and 2020, 80.5% (99/123) and 65.9% (27/41) of IPD cases in children under 5 years of age received at least one dose of the Pn13 vaccine. In 60 cases with a full vaccination schedule (3 doses) in 2019, 18 (30%) cases were vaccine failures (serotype Pn13), while of the 13 cases with full vaccination in 2020, 7 (54%) were vaccine failures (serotype Pn13).

4.9.2 Pneumococcal polysaccharide vaccine Pn23

Of the total number of IPD cases aged 65 years and over, 370 (62.3%) and 168 (66.1%) cases received the Pn23 vaccine, and of these, 79% and 78% of cases received the dose more than 5 years ago.

4.10 Antibiotic sensitivity

The percentages of cases with known antibiotic sensitivity were 77.7% (908/1168) and 71.5% (392/548) in 2019 and 2020, respectively. The antibiotic with the highest percentage of resistant strains was erythromycin, with values of 18.9% (172/908) in 2019 and 22.4% (88/392) in 2020, followed by penicillin with percentages of 2.8% and 2.3% in 2019 and 2020, respectively (figure 4). Cefotaxime presented resistance values of 0.9% and 0.3%, and levofloxacin of 0.4% and 1.0%, in 2019 and 2020, respectively.

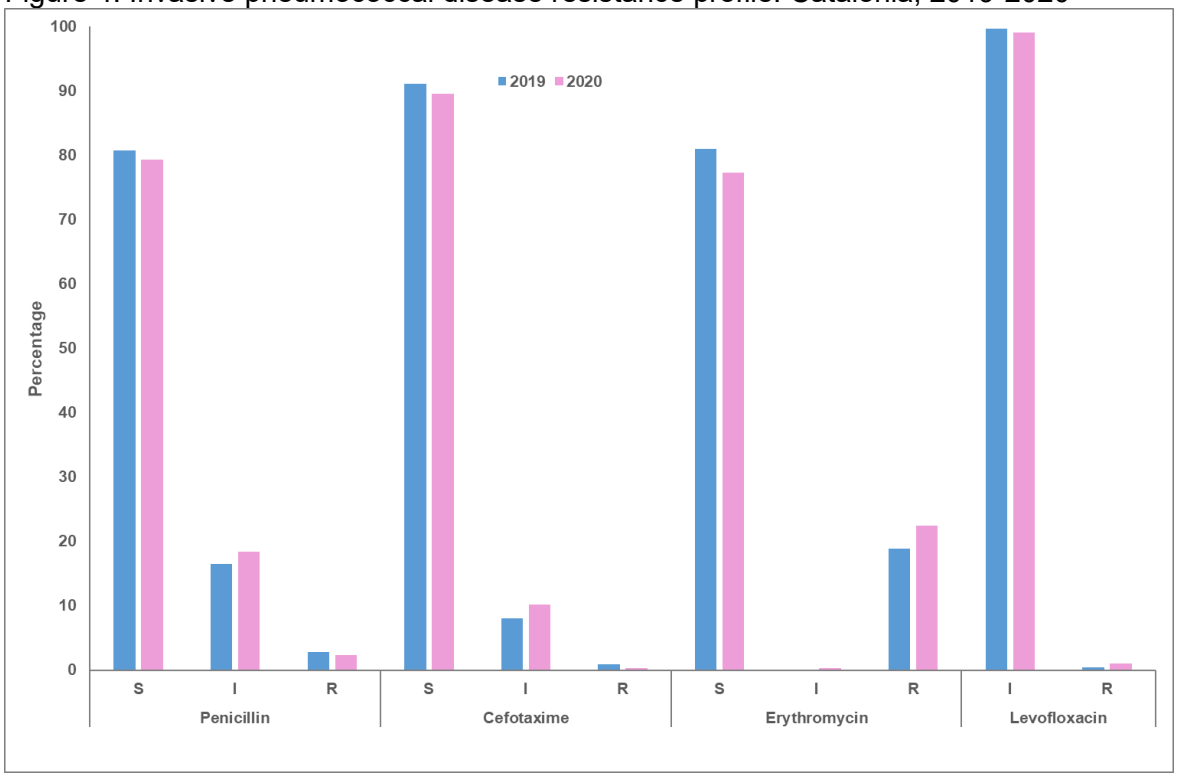
In 2019, the serotypes with the highest percentages of penicillin-resistant strains were 14 (16%, 4 cases), 11A (16%, 4 cases), 24F (12%, 3 cases) and 19A (8%, 2 cases), while in 2020 it was 11A (66.7%, 6 cases) (figure 5).

For cefotaxime, the serotype with the highest percentage of resistance was 14 (75%, 6 cases) in 2019 and 19A (1 strain) in 2020.

Between 2019 and 2020, erythromycin showed resistant strains with higher percentages in serotypes 24F (17.4%, 30 cases, and 18.2%, 16 cases, respectively), 33F (12.2%, 21 cases, and 11.4%, 10 cases, respectively) and 15A (12.2%, 21 cases, and 14.8%, 13 cases, respectively).

With regard to penicillin and erythromycin resistance, 12 cases (1.3%; 12/908) and 5 cases (1.3%; 5/392) submitted it in 2019 and 2020, respectively. In 2019, the serotypes were 14 (2 strains), 15A (1 strain), 19A (2 strains), 19F (1 strain), 23B (1 strain), 23F (1 strain), 24F (1 strain), 35B (1 strain), 6A (1 strain) and 6C (1 strain), 35B (1 strain), 6A (1 strain) and 6C (1 strain), while in 2020 the serotypes were 11A (2 strains), 19A (1 strain), 23A (1 strain) and 6C (1 strain). In 1 case (0.3%; 1/392) simultaneous resistance to penicillin, erythromycin and cefotaxime, caused by serotype 19A, was observed.

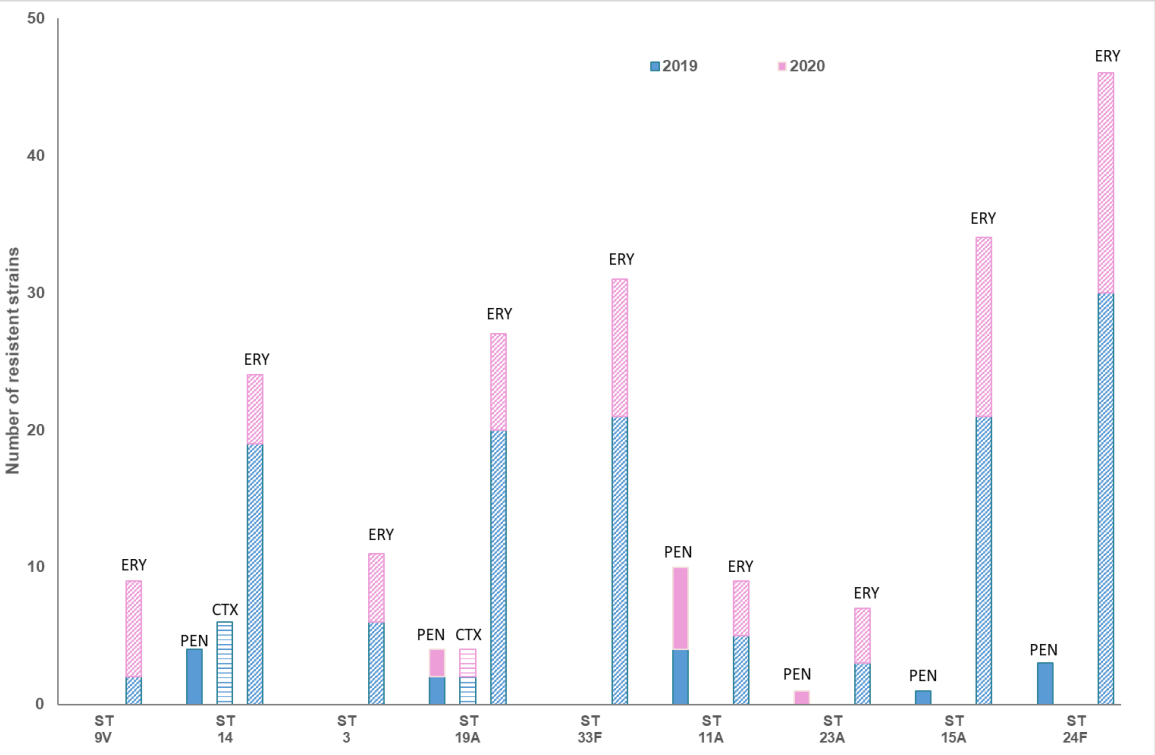
Figure 4. Invasive pneumococcal disease resistance profile. Catalonia, 2019-2020



Source: Microbiological Reporting System of Catalonia. Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.

S: Sensitive to standard dosage; I: Sensitive with increased exposure; R: High probability of therapeutic failure

Figure 5. Percentage of resistant strains of invasive pneumococcal disease by antibiotic, serotype and year. Catalonia, 2019-2020



Source: Microbiological Reporting System of Catalonia. Subdirectorate-General for Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia.

ST: serotype; PEN: penicillin; CTX: cefotaxime; ERY: erythromycin

5 Conclusions

5.1 2019 and 2020

- The overall incidence rate of IPD during 2019 and 2020 was 15.2 and 7.0 cases per 100,000 inhabitants, respectively, with a 46% reduction in 2020 compared to 2019. The restriction measures taken during the COVID-19 pandemic in 2020 probably contributed significantly to this reduction overall, across all age groups and across serotype groups included or not included in the Pn13 conjugate vaccine.

- Overall, the age group with the highest incidence of IPD was adults aged 65 years and over, followed by children under 5 years of age.

- Pneumonia was the most frequent clinical manifestation in all age groups, with higher incidence rates in adults aged 65 years. Meningitis showed higher incidence rates in children under 5 years of age.

- Of the total number of cases, 66.4% and 68.1% presented an underlying medical condition in 2019 and 2020, respectively, mainly in those aged 65 and over.

- Of the total number of reported cases, 89.0% required hospital admission in 2019 and 88.5% in 2020. The case fatality rate was 13.0% in 2019 and 12.6% in 2020.

- Overall, the most frequent circulating serotypes were serotypes 8, 3, 12F (included in Pn20) and 24F (not included in any vaccine).

- In 2019, serotypes included in the Pn13, Pn15 and Pn20 vaccines in children under 5 years of age accounted for 31.1%, 35.0% and 55.3%, respectively. In 2020, serotypes included in the Pn13, Pn15 and Pn20 vaccines accounted for 25.7%, 31.4% and 48.6%, respectively.

- In adults aged 65 years and older, serotypes included in the Pn13, Pn15, Pn20 and Pn23 vaccines accounted for 26.5%, 35.2%, 64.8% and 70.4%, respectively, in 2019, while in 2020 they accounted for 23.8%, 31.0%, 52.9% and 61.9%, respectively.

- The serotypes with the highest fatality rates were 3 (2019: 10.7%; 2020: 9.8%) and 8 (2019: 7.4%; 2020: 15.7%).

- The antibiotic with the highest percentage of resistant strains was erythromycin, with values of 18.9% in 2019 and 22.4% in 2020, followed by penicillin, with percentages of 2.8% and 2.3% in 2019 and 2020, respectively. Serotypes with the highest percentage of resistant strains were 24F, 33F and 15A.

- Of the 60 cases of IPD in children <5 years with a full vaccination schedule in 2019, 18 cases were vaccine failures, while of the 13 cases with full vaccination in 2020, 7 cases were vaccine failures.

5.2 Analysis of years 2017-2020 compared to 2016

- Between 2017 and 2019, increases of 10% and 15% were observed in the overall incidence rate compared to 2016, mainly caused by serotypes not included in the Pn13 vaccine, whereas in 2020, a significant reduction in the incidence of IPD (54%) was observed compared to 2016, both for Pn13 serotypes (54%) and non-Pn13 serotypes (40%).

- In children under 5 years of age, the incidence of IPD remains stable and no significant changes in the serotypes included in the Pn13 and non-Pn13 vaccine were observed when comparing years 2017-2019 with 2016, mainly due to the persistence of serotype 3 and 24F. However, a 67% decrease in incidence of serotypes included in the Pn13 vaccine and a 46% decrease in the non-Pn13 serotypes were observed in 2020.

- The increase in incidence was significant in the 20-64 age group (between 20% and 31%) only in years 2017 and 2019 mainly due to the increase of the serotypes included in Pn13. In contrast, in 2020 there was a decrease in the incidence rate in both serotype groups (Pn13 and non-Pn13).

- In the 65 and older age group, an increase was observed in the incidence of non-Pn13 serotypes of 19% (in 2018) and 41% (in 2019), mainly due to the increase of serotype 8, while 2020 showed a decrease in the incidence of Pn13 (59%) and non-Pn13 (41%) serotypes.

There is a need to strengthen the accurate and timely reporting of IPD cases and serotypes by laboratories in Catalonia to the SNMC.

It is important to maintain homogeneous and continuous epidemiological surveillance of IPD to detect changes in the epidemiology and distribution of circulating serotypes in order to assess the potential impact of pneumococcal vaccines.

6 References

1. Interterritorial Board of the National Health System. Common vaccination Schedule across life. Available at: Recommended vaccination schedule, 2020.

2. Recommendad schedule for routine vaccination, 2016 [poster]. Barcelona: Ministry of Health; 2016. Available at: Systematic vaccination schedule 2016.

3. Decree 203/2015, of 15 de September, creating the Epidemiological Surveillance Network of Catalonia and regulating reporting systems for notifiable diseases and epidemic outbreaks. Diari Oficial de la Generalitat de Catalunya. 2015 17 set;6958. Available at: Decree 203/2015.

4. SpIDnet project [Internet]. European Centre for Disease Prevention and Control. Available at: SpIDnet.

5. Domínguez A, Ciruela P, García-García JJ et al. Effectiveness of 7-valent pneumococcal conjugate vaccine in the prevention of invasive pneumococcal disease in children aged 7-59 months. A matched case-control study. Vaccine 29 2011;29: 9020-9025

6. Domínguez A, Ciruela P, Hernández S et al. Effectiveness of the 13-valent pneumococcal conjugate vaccine in preventing invasive pneumococcal disease in children aged 7-59 months. A matched case-control study. PLoSONE 12(8):e0183191.

7. Savulescu C, Krizova P, Valentiner-Branth P, et al. Effectiveness of 10 and 13-valent pneumococcal conjugate vaccines against invasive pneumococcal disease in European children: SpIDnet observational multicentre study. Vaccine 2022; 40:3963-3974.

8. Ciruela P, Izquierdo C, Broner S, et al. The changing epidemiology of invasive pneumococcal disease after PCV13 vaccination in a country with intermediate vaccination coverage. Vaccine. 2018;36: 7744-7752.

9. Ciruela P, Broner S, Izquierdo C, et al. Indirect effects of paediatric conjugate vaccines on invasive pneumococcal disease in older adults. Int J Infect Dis. 2019; 86: 122-130.

10. Hanquet G, Krizova P, Valentiner-Branth P et al. Effect of childhood pneumococcal conjugate vaccination on invasive disease in older adults of 10 European countries: implications for adult vaccination. Thorax 2018; 0:1-10.

11. Deloria Knoll M, Bennett J, Gracia Quesada M et al. Global Landscape Review of Serotype-Specific Invasive Pneumococcal Disease Surveillance among Countries Using PCV10/13: The Pneumococcal Serotype Replacement and Distribution Estimation (PSERENADE) Project. Microorganisms 2021; 9:742.

12. Bennett J, Hetrich M, Garcia Quesada M et al. Changes in Invasive Pneumococcal Disease Caused by *Streptococcus pneumoniae* Serotype 1 Following Introduction of PCV10 and PCV13: Findings from the PSERENADE Project. Microorganisms 2021; 9:696.

13. Garcia Quesada M, Yang Y, Bennett J et al. Serotype Distribution of Remaining Pneumococcal Meningitis in the Mature PCV10/13 Period: Findings from the PSERENADE Project. Microorganisms 2021; 9:738.

14. Broner S, Izquierdo C, Nogueras MM et al. Impacto de la vacuna antineumocócica conjugada 13-valente en la incidencia de la enfermedad neumocócica invasiva en Cataluña: Estudio retrospectivo, 2014-2015 vs. 2017-2018. Vacunas 2022; 23:32-41.

15. Centers for Disease Control and Prevention (CDC). Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2012; 61: 816-9.

16. Klugman KP, Rodgers GL. Time for a third-generation pneumococcal conjugate vaccine. Lancet Infect Dis. 2021; 21:14-16.

17. EUCAST. The European Committee on Antimicrobial Susceptibility Testing. Eur Comm Antimicrob Susceptibility Test [Internet]. 2015;0-77. Available at: http://www.eucast.org.

18. Subdirectorate-General of Epidemiological Surveillance and Public Health Emergency Response. Public Health Agency of Catalonia. Protocol de vigilància de les resistències antimicrobianes a Catalunya. 2015;1-34. Available at: https://scientiasalut.gencat.cat/handle/11351/2601?locale-attribute=es

19. Ministry of Health. Government of Spain. Coverage of vaccination. Year 2020. https://pestadistico.inteligenciadegestion.sanidad.gob.es/publicoSNS/I/sivamin/sivamin (accessed 10 Oct 2022).

20. Vila-Córcoles A, Ochoa-Gondar O, de Diego C et al. Pneumococcal vaccination coverages by age, sex and specific underlying risk conditions among middle-aged and older adults in Catalonia, Spain, 2017. Euro Surveill. 2019; 24:1800446.

21. Ciruela P, Soldevila N, García-Garcia JJ et al. Effect of COVID-19 Pandemic on Invasive Pneumococcal Disease in Children, Catalonia, Spain. Emerg Infect Dis 2022; 28: 2321-2325.

7 **Annex 1. Laboratories reporting to SNMC** and participating hospitals, year 2020

Catlab-Centre Analítiques Terrassa, AIE	Fundació Hospital Sant Joan de Déu (Martorell) Hospital de Terrassa Hospital Universitari Mútua de Terrassa
Consorci del Laboratori Intercomarcal de L'Alt Penedès	Hospital Comarcal de Vilafranca del Penedès Hospital de Sant Joan Despí Moisès Broggi Hospital d'Igualada Hospital Dos de Maig Hospital General de L'Hospitalet Hospital Residència Sant Camil - Consorci Sanitari Hospital Sant Antoni Abat - Consorci Sanitari de l
Fundació Hospital de l'Esperit Sant	Fundació Hospital de l'Esperit Sant
Hospital de Barcelona	Hospital de Barcelona
Hospital Clínic de Barcelona	Hospital Clínic de Barcelona Hospital Clínic de Barcelona, Seu Sabino De Arana
Hospital Comarcal de Sant Bernabé	Hospital Comarcal de Sant Bernabé
Hospital Comarcal Móra d'Ebre	Hospital Comarcal Móra d'Ebre
Corporació de Salut del Maresme i La Selva	Hospital Comarcal de Blanes Hospital Comarcal Sant Jaume de Calella
Hospital de Cerdanya / Hôpital de Cerdagne	Hospital de Cerdanya / Hôpital de Cerdagne
Hospital de Figueres	Hospital de Figueres
Hospital de la Santa Creu i Sant Pau	Hospital de la Santa Creu i Sant Pau Fundació Puigvert - IUNA
Hospital de Mataró	Hospital de Mataró
Hospital de Palamós	Hospital de Palamós
Hospital de Sabadell	Hospital de Sabadell
Hospital de Sant Joan de Déu (Manresa) - Althaia	Hospital de Sant Joan de Déu (Manresa) - Althaia Clínica Sant Josep Centre Hospitalari Manresa-Fundació ALTHAIA
Hospital de Sant Joan de Déu - Esplugues	Hospital de Sant Joan de Déu - Esplugues
Hospital de Sant Pau i Santa Tecla	Hospital de Sant Pau i Santa Tecla Hospital del Vendrell
Hospital de Tortosa Verge de la Cinta	Hospital de Tortosa Verge de la Cinta
Hospital d'Olot i Comarcal de la Garrotxa	Hospital d'Olot i Comarcal de la Garrotxa
Hospital General de Granollers	Hospital General de Granollers
Hospital Municipal de Badalona	Hospital Municipal de Badalona
Hospital Universitari Arnau de Vilanova de Lleida	Hospital Universitari Arnau de Vilanova de Lleida Hospital Santa Maria

Catlab-Centre Analítiques Terrassa, AIE	Fundació Hospital Sant Joan de Déu (Martorell) Hospital de Terrassa Hospital Universitari Mútua de Terrassa
Hospital Universitari de Bellvitge	Hospital de Viladecans Hospital Universitari de Bellvitge Hospital Duran i Reynals
Hospital Universitari de Girona Dr. Josep Trueta	Hospital Universitari de Girona Dr. Josep Trueta Hospital de Campdevànol Hospital Santa Caterina-IAS
Hospital Universitari de Sant Joan de Reus	Hospital Comarcal d'Amposta Hospital Universitari de Sant Joan de Reus
Hospital Universitari de Vic	Hospital de Sant Jaume Hospital Universitari de Vic
Hospital Universitari General de Catalunya	Hospital Universitari General de Catalunya
Hospital Universitari General de la Vall d'Hebron	Hospital Universitari General de la Vall d'Hebron Hospital de Mollet
Hospital Universitari Germans Trias i Pujol de Badalona	Hospital Universitari Germans Trias i Pujol de Badalona
Hospital Universitari Joan XXIII de Tarragona	Hospital Universitari Joan XXIII de Tarragona Pius Hospital de Valls
Laboratori de Referència de Catalunya	Hospital de l'Esperança Hospital de Sant Celoni Hospital del Mar Hospital Comarcal Sant Jaume de Calella* Hospital Comarcal de Blanes* Hospital de Mataró* Hospital Municipal de Badalona* Clínica Terres de l'Ebre Hospital Universitari de Sant Joan de Reus*
Parc Sanitari Sant Joan de Déu - Hospital General	Parc Sanitari Sant Joan de Déu - Hospital General
SYNLAB Diagnósticos Globales	

*For some determinations