Analysis of the Antimicrobial Resistance Profile of Microorganisms Closely Related to Healthcare-Associated Infections. Catalonia, 2016-2019

Microbiological Reporting System of Catalonia

Sub-directorate General for Public Health Emergency Surveillance and Response

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Contents

1 Introduction

Acquisition of antibiotic resistance by bacteria causing infectious diseases is one of today's major public health problems as it restricts the treatment of diseases due to reduced efficacy of drugs and compels continuous review of and change in therapeutic treatments. The World Health Organisation has identified antimicrobial resistance as one of the top 10 public health threats we face. In the European Union, 33,000 deaths per year on average are a direct consequence of infections caused by antibiotic-resistant bacteria resulting in additional healthcare expenditure coming to €1.5 billion per year (1-3). Resistance to last-line antibiotics such as carbapenems and colistin (1) causes 39% of these infections. If no action is taken, it is estimated that in 35 years deaths due to infections caused by multidrug-resistant bacteria would increase to around 10 million per year globally of which 390,000 would be in Europe and 40,000 in Spain, thus making it the leading cause of death ahead of cancer (2,4,5).

Healthcare-associated infections (HAIs) resulting from resistant bacteria are a major cause of mortality and morbidity (6). One study shows that 63.5% of infections due to resistant bacteria in the European Union are HAI-related accounting for 72.4% of deaths and this mortality is rising (1). *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pneumoniae, Acinetobacter baumannii* and *Pseudomonas aeruginosa* are the six leading microorganisms for deaths from antibiotic-resistant infections (7). Indeed, these six microorganisms were responsible for almost 80% of the 1.27 million deaths directly attributed to antibiotic resistance in 2019 (4). In Spain and the European Union, the European Antimicrobial Resistance Surveillance-Network (EARS-Net) monitors these microorganisms along with enterococci (1,3).

Controlling antibiotic-resistant strains takes a single health approach and is anchored in several work strands: surveillance, control, prevention, research, education and communication (5). Surveillance of the spread of resistant strains makes it possible to analyse trends over time and space, providing information that is or can be used in decisions on the control and treatment of these infections (8).

In Catalonia, reporting antibiotic resistance is compulsory under Decree 203/2015 of 15 September and Order SLT/205/2019 of 19 November. The Decree set up the Epidemiological Surveillance Network of Catalonia and regulates the reporting system for notifiable diseases and epidemic outbreaks. It also established the Microbiological Reporting System of Catalonia (SNMC) as the system that compiles notifiable microorganisms and their antimicrobial resistance (9). Order SLT/205/2019 of 19 November expanded the list of microorganisms to include healthcare-associated infections and extended the surveillance of their antibiotic resistance (10).

In 2015, the Protocol for the surveillance of antibiotic resistance in Catalonia was published with the consensus of the SNMC working group (8). This Protocol

specifies the microorganisms and antibiotics subject to surveillance. The microorganisms have to cause acute infectious disease with the analytical confirmation, specified in *Diagnostic Criteria for Microorganisms Reported in the Microbiological Reporting System of Catalonia – 2015 update* (11). These criteria follow the international standards of the ECDC and have been reviewed by the Sub-directorate General for Public Health Emergency Surveillance and Response (SGVRESP) professionals and SNMC working group microbiologists to tailor them to our setting. Likewise, the cut-off points for the follow-up and monitoring of antimicrobial resistance are those recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

2 Objective

The purpose of this report is to analyse the antimicrobial susceptibility of microorganisms closely related to HAIs. It also examines their resistance mechanisms and the presence of multidrug-resistant, extensively drug-resistant and pandrug-resistant strains in the years 2016-2019. The microorganisms under study are gram-positive cocci: *Enterococcus faecalis, Enterococcus faecium, Streptococcus agalactiae, Streptococcus pyogenes* and *Staphylococus aureus* (MSSA and MRSA); enterobacteriaceae: *Escherichia coli* and *Klebsiella pneumoniae*, and non-fermenting gram-negative bacilli: *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.

3 Methods

3.1 Participating centres

The information analysed refers to cases of patients who were treated or admitted to hospital and out-of-hospital care facilities in Catalonia and had a confirmed episode of acute infectious disease caused by the microorganisms under study.

Forty-one centres reported antibiotic resistance data for the period under study (Annex 1). Thirty-one of these centres detected resistance mechanisms and 12 detected multidrug-resistant strains.

3.2 Data collection

The surveillance protocol stipulates that data collection on the antibiotic resistance of microorganisms closely related to HAIs have to be collected annually and aggregated . Centres report the number of strains tested and specify the number of strains that are susceptible, intermediate or resistant to the antibiotics under surveillance.

Furthermore, centres that have the capacity to detect resistance mechanisms together with multidrug-resistant, extensively drug-resistant and pandrug-resistant strains also report these data. We define a microorganism as multidrug-resistant (MDR) when it shows no susceptibility to at least one antibiotic from three or more families considered useful for the treatment of its infections; as extensively drug-

resistant (XDR) when it shows no susceptibility to at least one antibiotic from all but one or two families; and as pandrug-resistant (PDR) when it shows no susceptibility to all antibiotics from all families commonly used for treatment (12). The antibiotics and resistance mechanisms tested for each microorganism are shown in Annex 2.

These data are collected using a specific annual form, which each centre sends to the SNMC in the Sub-directorate General for Public Health Emergency Surveillance and Response (SGVRESP) at the Public Health Agency of Catalonia (ASPCAT) which coordinates the surveillance.

The data have to meet the following criteria for all microorganisms:

- Usually sterile specimen (CSF, blood, serum, pleural fluid, peritoneal fluid, joint fluid, bone tissue, etc.).
- Only one specimen per patient and infectious process should be reported.
- Colonisations should not be included.
- The cut-off points used should be those recommended by EUCAST following the annual updates.

Each centre is given a survey on these criteria to validate their compliance for each specific microorganism and antibiotic and reports that fail to do so are discarded. Overall, the data from six centres were discarded because they could not discriminate between sterile and non-sterile samples, those from one centre did not differentiate between colonisations and acute infections, one centre did not answer the survey, and another used the cut-off points of the American CLSI (Clinical and Laboratory Standards Institute) guide.

3.3 Analysis

A descriptive and retrospective analysis of laboratory-confirmed case reports from 2016-2019 was performed. The total number of strains tested by resistance profile per year of study was analysed.

The number of strains for which the study of resistance mechanisms was conducted and the number of positives and negatives per study year were analysed. Finally, the number of strains in which resistance mechanisms were detected and the number of multidrug-resistant, extensively drug-resistant and pandrug-resistant strains were examined.

The variation in the percentage of resistant strains and the percentage of susceptible strains in 2019 compared to 2016 was calculated using statistical analysis of comparison of proportions by independent samples using the Epidat 3.1program. Values of p <0.05 were considered statistically significant.

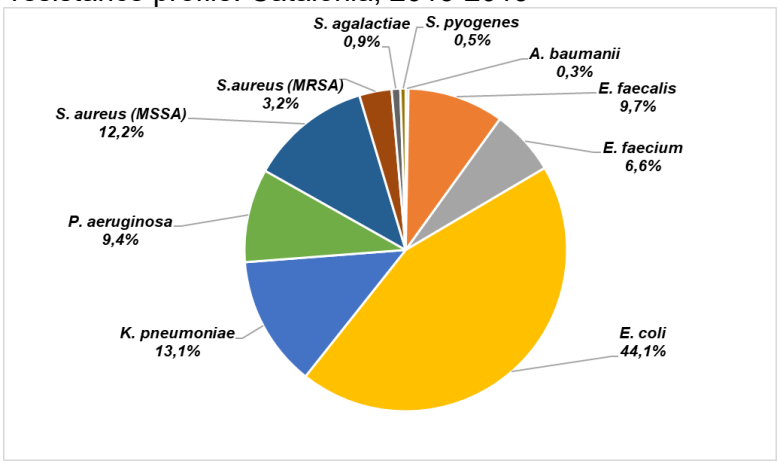
4 Results

4.1 Data analysed

A total of 173,990 antibiotic resistance tests performed on 21,062 strains isolated in the period 2016-2019 were reported.

The highest percentage of isolates was *Escherichia coli* (44.1%) followed by *Klebsiella pneumoniae* (13.1%). Less than 5% of isolates were *Staphylococcus aureus* MRSA, *Streptococcus agalactiae*, *Streptococcus pyogenes* and *Acinetobacter baumannii* (Figure 1).

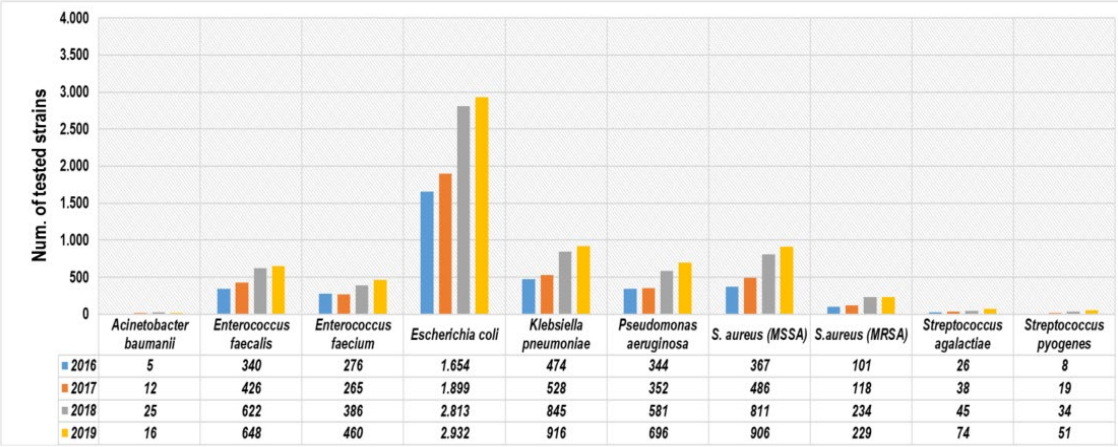
Figure 1. Distribution by microorganism of the percentage of strains tested with detection of antimicrobial-resistance profile. Catalonia, 2016-2019



Source: SNMC. SGVRESP. ASPCAT.

The number of strains tested and the number of antibiotic susceptibility tests performed per microorganism and year are shown in figures 2 and 3.

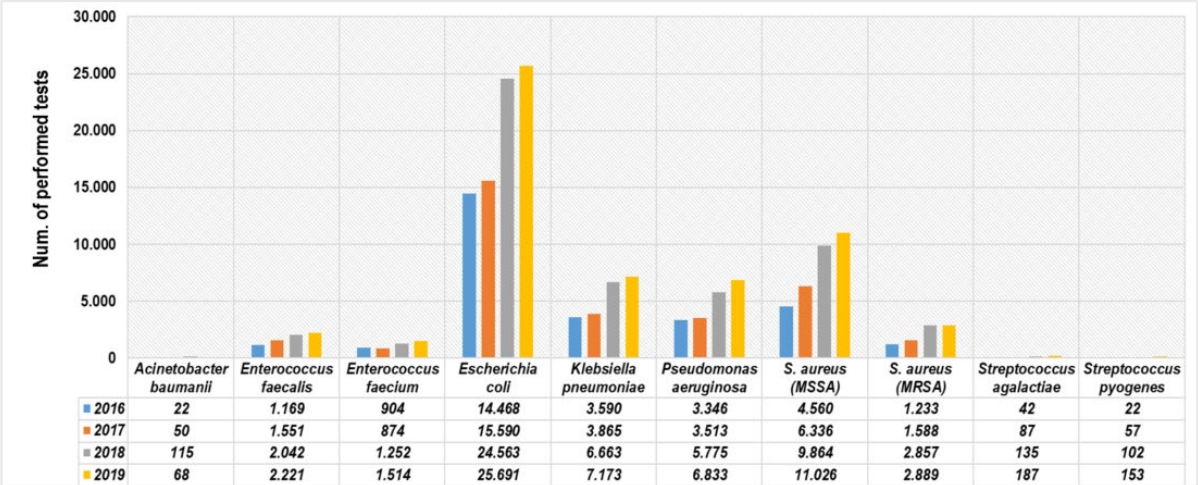
Figure 2. Number of strains tested by microorganism and year. Catalonia, 2016-2019



	Acinetobacter baumanii	Enterococcus faecalis	Enterococcus faecium	Escherichia coli	Klebsiella pneumoniae	Pseudomonas aeruginosa	S. aureus (MSSA)	S.aureus (MRSA)	Streptococcus agalactiae	Streptococcus pyogenes
2016	5	340	276	1.654	474	344	367	101	26	8
2017	12	426	265	1.899	528	352	486	118	38	19
2018	25	622	386	2.813	845	581	811	234	45	34
2019	16	648	460	2.932	916	696	906	229	74	51

Source: SNMC. SGVRESP. ASPCAT.

Figure 3. Number of antibiotic susceptibility tests performed by microorganism and year. Catalonia, 2016-2019

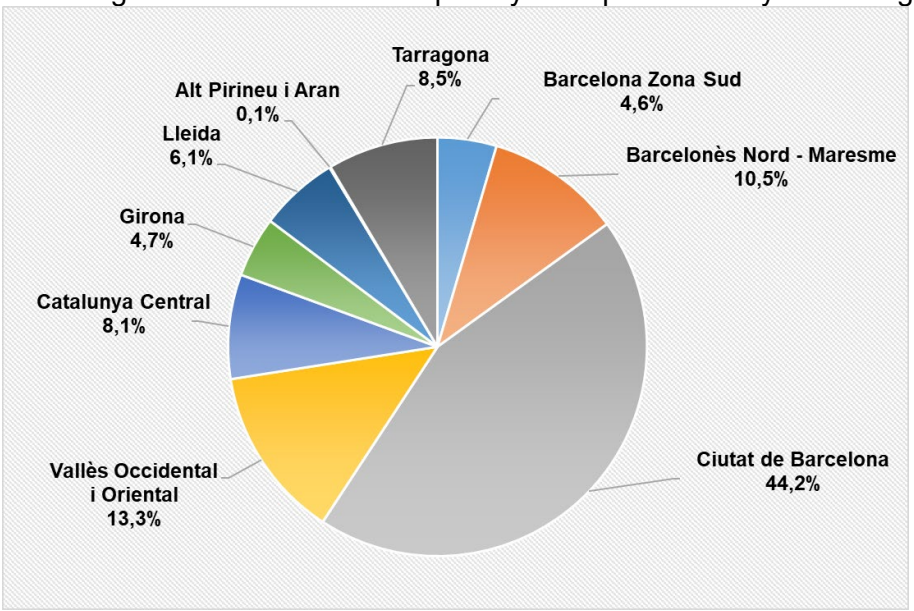


	Acinetobacter baumanii	Enterococcus faecalis	Enterococcus faecium	Escherichia coli	Klebsiella pneumoniae	Pseudomonas aeruginosa	S. aureus (MSSA)	S. aureus (MRSA)	Streptococcus agalactiae	Streptococcus pyogenes
2016	22	1.169	904	14.468	3.590	3.346	4.560	1.233	42	22
2017	50	1.551	874	15.590	3.865	3.513	6.336	1.588	87	57
2018	115	2.042	1.252	24.563	6.663	5.775	9.864	2.857	135	102
2019	68	2.221	1.514	25.691	7.173	6.833	11.026	2.889	187	153

Source: SNMC. SGVRESP. ASPCAT.

Strains from the entire territory and health regions were analysed. Figure 4 shows the distribution by territory of the antibiograms performed considering the location of the reporting laboratory.

Figure 4. Percentage of antimicrobial susceptibility tests performed by health region



Source: SNMC. SGVRESP. ASPCAT.

4.2 Monitoring antibiotic susceptibility and mechanisms of resistance: gram-positive cocci

4.2.1 Enterococcus faecalis

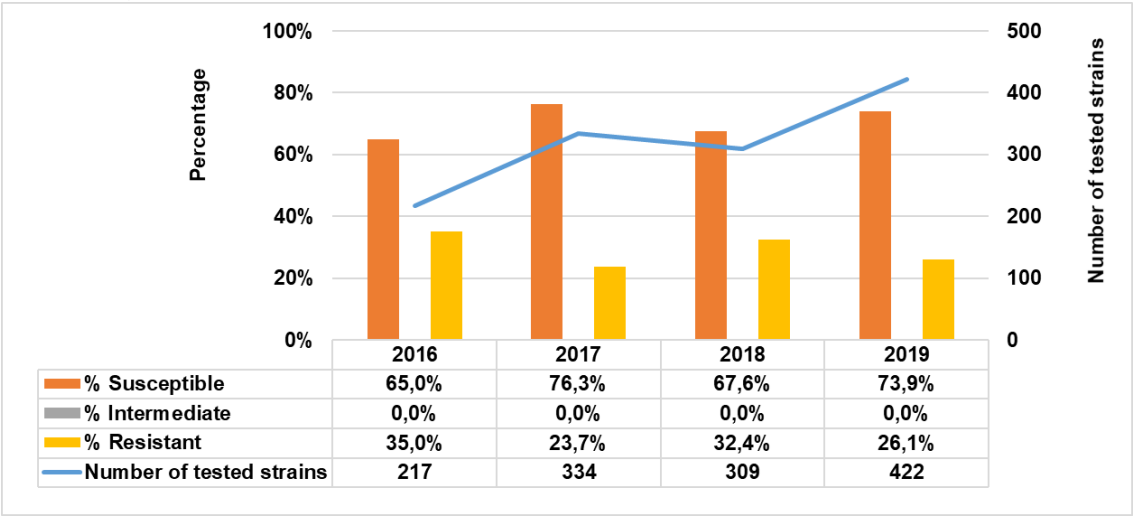
Antibiotic susceptibility of *Enterococcus faecalis* to ampicillin, streptomycin, gentamicin and vancomycin was tested.

In the study period, seven strains with ampicillin resistance were reported: 2/340 (0.6%) in 2016, 4/622 (0.6%) in 2018 and 1/648 (0.2%) in 2019. No resistant strains were detected in 2017 (number of strains tested: 425).

Regarding high-level resistance to aminoglycosides, 28.5% (365/1,282) of the total strains were resistant to streptomycin and 30.0% (497/1,659) to gentamicin.

Figures 5 and 6 show the distribution of susceptibility to these antibiotics by year. There was a statistically significant reduction of 25.6% in the percentage of resistance to streptomycin in 2019 compared to 2016 (p = 0.0233). The decrease in the percentage of strains resistant to gentamicin (14.0%) in 2019 was not statistically significant.

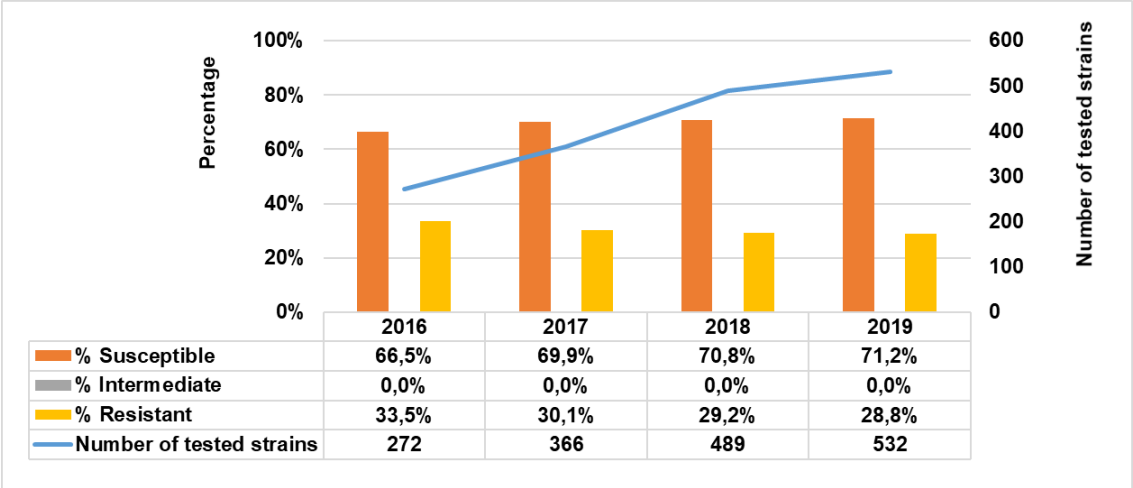
Figure 5. Evolution of antibiotic susceptibility of *Enterococcus faecalis* to streptomycin. Catalonia, 2016-2019



	2016	2017	2018	2019
% Susceptible	65,0%	76,3%	67,6%	73,9%
% Intermediate	0,0%	0,0%	0,0%	0,0%
% Resistant	35,0%	23,7%	32,4%	26,1%
Number of tested strains	217	334	309	422

Source: SNMC. SGVRESP. ASPCAT.

Figure 6. Evolution of antibiotic susceptibility of *Enterococcus faecalis* to gentamicin. Catalonia, 2016-2019



	2016	2017	2018	2019
% Susceptible	66,5%	69,9%	70,8%	71,2%
% Intermediate	0,0%	0,0%	0,0%	0,0%
% Resistant	33,5%	30,1%	29,2%	28,8%
Number of tested strains	272	366	489	532

Source: SNMC. SGVRESP. ASPCAT.

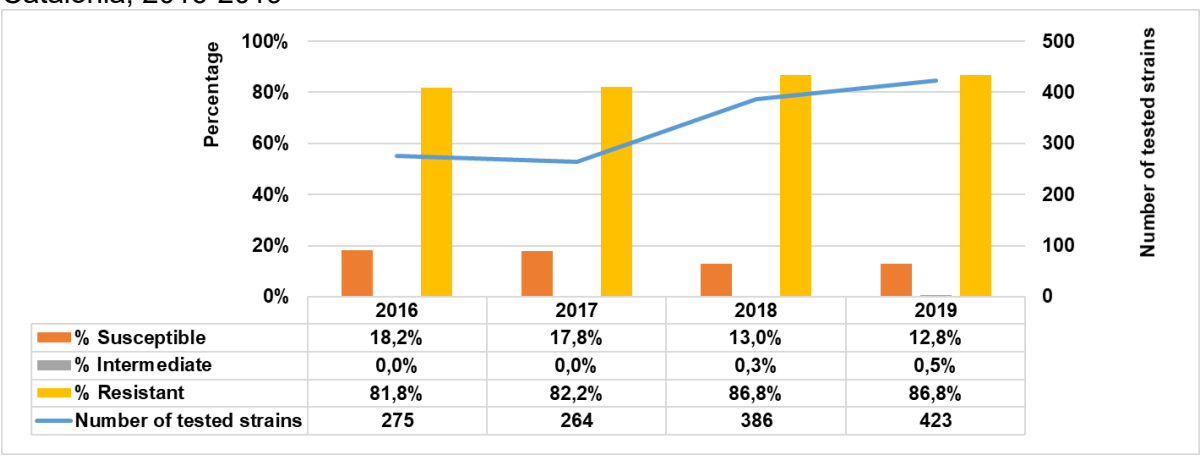
No vancomycin-resistant strains were isolated in the whole period (strains tested: 340 in 2016, 426 in 2017, 622 in 2018 and 619 in 2019).

4.2.2 Enterococcus faecium

Antibiotic susceptibility of *Enterococcus faecium* to ampicillin, streptomycin, gentamicin and vancomycin was tested.

Overall, 84.9% (1,144/1,348) of strains over the entire period were resistant to ampicillin. The percentages of resistant and susceptible strains remained the same over time with no statistically significant differences (Figure 7).

Figure 7. Evolution of antibiotic susceptibility of *Enterococcus faecium* to ampicillin. Catalonia, 2016-2019

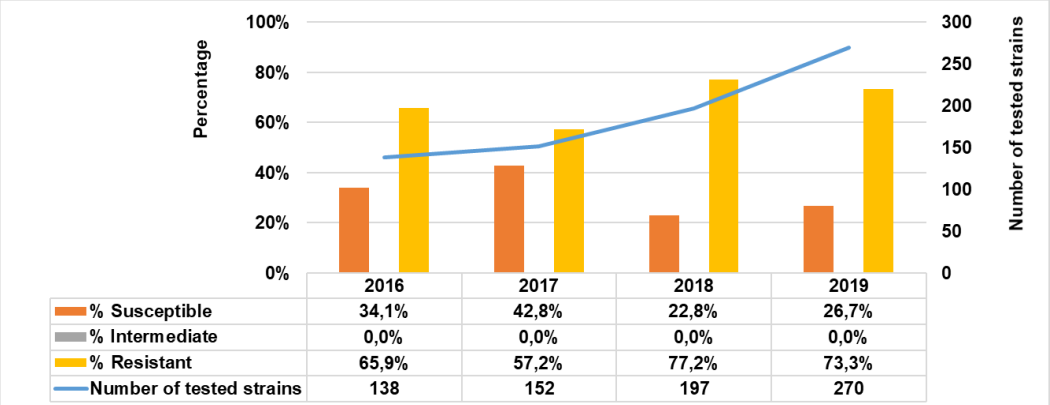


	2016	2017	2018	2019
% Susceptible	18,2%	17,8%	13,0%	12,8%
% Intermediate	0,0%	0,0%	0,3%	0,5%
% Resistant	81,8%	82,2%	86,8%	86,8%
Number of tested strains	275	264	386	423

Source: SNMC. SGVRESP. ASPCAT.

Overall, high-level resistance to streptomycin was 69.7% (528/757). Figure 8 shows the evolution by year. There was a slight increase of 11.2% in the percentage of resistance in 2019 compared to 2016 (not significant, $p = 0.1502$).

Figure 8. Evolution of antibiotic susceptibility of *Enterococcus faecium* to streptomycin. Catalonia, 2016-2019

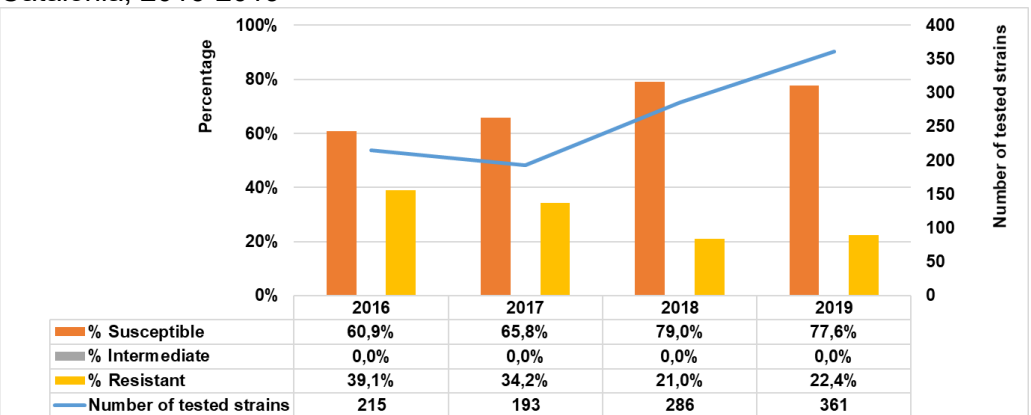


	2016	2017	2018	2019
% Susceptible	34,1%	42,8%	22,8%	26,7%
% Intermediate	0,0%	0,0%	0,0%	0,0%
% Resistant	65,9%	57,2%	77,2%	73,3%
Number of tested strains	138	152	197	270

Source: SNMC. SGVRESP. ASPCAT.

Overall, 27.6% (291/1,055) of strains tested in the study period were high-level resistant to gentamicin. There was a 42.6% decrease in gentamicin resistance in 2019 compared to 2016 ($p < 0.001$) (Figure 9).

Figure 9. Evolution of antibiotic susceptibility of *Enterococcus faecium* to gentamicin. Catalonia, 2016-2019



	2016	2017	2018	2019
% Susceptible	60,9%	65,8%	79,0%	77,6%
% Intermediate	0,0%	0,0%	0,0%	0,0%
% Resistant	39,1%	34,2%	21,0%	22,4%
Number of tested strains	215	193	286	361

Source: SNMC. SGVRESP. ASPCAT.

The antibiotic susceptibility profile for vancomycin was tested in 1,384 isolates: 276 in 2016, 265 in 2017, 383 in 2018 and 460 in 2019. The presence of resistance mechanisms (VanA and VanB phenotypes) was tested in 498 (35.9%) isolates: 193 (69.9%) in 2016, 106 (40.0%) in 2017, 144 (37.6%) (VanA phenotype) and 54 (14.1%) (VanB phenotype) in 2018, and 55 (11.9%) in 2019.

Two vancomycin-resistant strains were detected: one strain in 2016 positive for the VanB phenotype (1/193; 0.5%) and one in 2018 positive for the VanA phenotype (1/144; 0.7%).

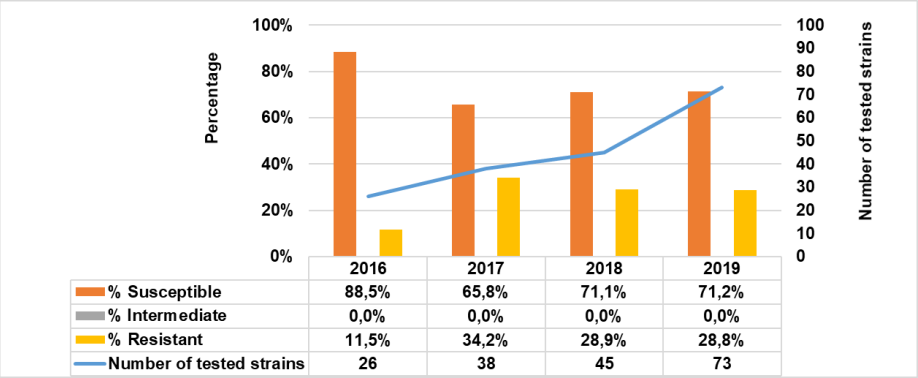
4.2.3 *Streptococcus agalactiae*

Streptococcus agalactiae was tested for susceptibility to benzylpenicillin, clindamycin and erythromycin.

No benzylpenicillin-resistant strains were detected during the entire period (strains tested: 11 in 2016, 24 in 2017, 45 in 2018 and 40 in 2019).

The overall percentage of isolates resistant to clindamycin was 27.5% (50/182). The evolution by year is shown in Figure 10. From 2016 to 2019, clindamycin-resistant strains rose from 11.5% to 28.8% (statistically non-significant, p = 0.1352).

Figure 10. Evolution of antibiotic susceptibility of *Streptococcus agalactiae* to clindamycin. Catalonia, 2016-2019

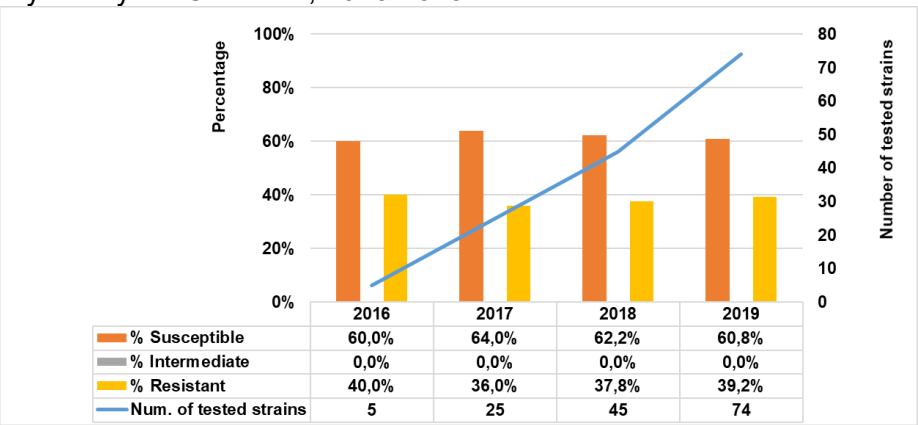


	2016	2017	2018	2019
% Susceptible	88,5%	65,8%	71,1%	71,2%
% Intermediate	0,0%	0,0%	0,0%	0,0%
% Resistant	11,5%	34,2%	28,9%	28,8%
Number of tested strains	26	38	45	73

Source: SNMC. SGVRESP. ASPCAT.

38.3% (57/149) of the strains were resistant to erythromycin. No statistically significant increase in erythromycin resistance in 2019 compared to 2016 was detected (Figure 11).

Figure 11. Evolution of antibiotic susceptibility of *Streptococcus agalactiae* to erythromycin. Catalonia, 2016-2019



	2016	2017	2018	2019
% Susceptible	60,0%	64,0%	62,2%	60,8%
% Intermediate	0,0%	0,0%	0,0%	0,0%
% Resistant	40,0%	36,0%	37,8%	39,2%
Num. of tested strains	5	25	45	74

Source: SNMC. SGVRESP. ASPCAT.

Across the 57 erythromycin-resistant strains in the study period, M phenotype was reported in 41 (71.9%): 14 in 2018 and 27 in 2019. Three (11.1%) strains were positive in 2019. Positive for the MLSB phenotype were: 1 out of 1 strain in 2017 (iMLSB/cMLSB could not be determined); 3 (17.6%) out of 17 strains in 2018 (2 cMLSB and 1 iMLSB) and 5 (11.6%) out of 43 strains (1 cMLSB and 4 iMLSB) in 2019.

4.2.4 Streptococcus pyogenes

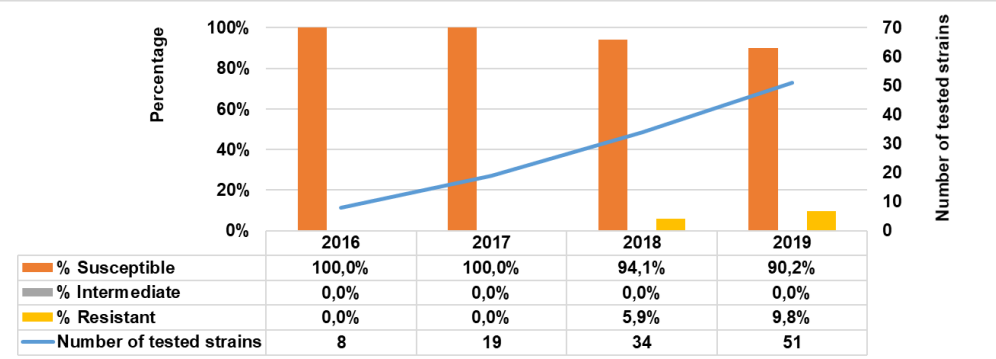
Streptococcus pyogenes was tested for susceptibility to benzylpenicillin, clindamycin and erythromycin.

For benzylpenicillin, 6 strains were tested in 2016, 19 in 2017, 34 in 2018 and 51 in 2019, and no resistant strains were detected.

As for clindamycin, 8 strains were tested in 2016, 19 in 2017, 34 in 2018 and 51 in 2019, of which 1 strain was resistant in 2018 (1/34; 2.9%).

As regards erythromycin, 7/112 (6.3%) resistant strains were detected: 2/34 strains (5.9%) in 2018 and 5/51 strains (9.8%) in 2019 (Figure 12).

Figure 12. Evolution of antibiotic susceptibility of *Streptococcus pyogenes* to erythromycin. Catalonia, 2016-2019



	2016	2017	2018	2019
% Susceptible	100,0%	100,0%	94,1%	90,2%
% Intermediate	0,0%	0,0%	0,0%	0,0%
% Resistant	0,0%	0,0%	5,9%	9,8%
Number of tested strains	8	19	34	51

Source: SNMC. SGVRESP. ASPCAT

M phenotype was reported for 12 strains in 2017 and 1 strain in 2018. The latter was positive.

In terms of the presence of 23S rRNA methylase (MLSB), 12 strains were tested in 2017 and 1 in 2018. The latter was positive for the cMLSB phenotype.

4.2.5 Staphylococcus aureus

In total, 3,252 *Staphylococcus aureus* strains were tested of which 682 (21.0%) were methicillin-resistant S. *aureus* (MRSA) and 2,570 (79.0%) methicillin-susceptible S. *aureus* (MSSA). There was no significant difference in the percentage of MRSA in 2019 compared to 2016 (Table 1).

Table 1. *Staphylococcus aureus* isolates by year of study. Catalonia, 2016-2019.

	2016	2017	2018	2019
Total number *Staphylococcus aureus*	468	604	1045	1135
Number *S. aureus* (MRSA)	101	118	234	229
% *S. aureus* (MRSA)	21.6%	19.5%	22.4%	20.2%

Source: SNMC. SGVRESP. ASPCAT.

Overall, benzylpenicillin resistance occurred in 89.7% (2,033/2,267) of S. *aureus* MSSA and 100% (621/621) of MRSA and remained constant over the years (Table 2).

The percentage of quinolone-resistant strains was below 10% in MSSA (7.1% (131/1,854) to ciprofloxacin and 5.9% (104/1,767) to levofloxacin) and above 80% in MRSA (87.1% (478/549) to ciprofloxacin and 87.0% (403/463) to levofloxacin).

There were no statistically significant variations between 2016 and 2019 in the percentage of strains resistant and susceptible to the two quinolones, although levofloxacin-resistant MSSA strains increased by 25.4% in 2019 compared to 2016 (Table 2).

Table 2. Evolution of antibiotic susceptibility of *Staphylococcus aureus* to β-lactams (benzylpenicillin [BP]) and quinolones (ciprofloxacin [CIP], levofloxacin [LEV]). Catalonia, 2016-2019

		MSSA 2016	MSSA 2017	MSSA 2018	MSSA 2019	MRSA 2016	MRSA 2017	MRSA 2018	MRSA 2019
BP	**R (%) #**	90.7%	93.3%	88.9%	87.7%	100%	100%	100%	100%
	I (%)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	S (%)	9.3%	6.7%	11.1%	12.3%	0%	0%	0%	0%
	N	*300*	*481*	*705*	*781*	*67*	*118*	*211*	*225*
CIP	**R (%)**	7.1%	7.0%	7.0%	7.1%	88.8%	81.2%	89.1%	87.7%
	I (%)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	S (%)	92.9%	93.0%	93.0%	92.9%	11.3%	18.8%	10.9%	12.3%
	N	*281*	*384*	*543*	*646*	*80*	*101*	*165*	*203*
LEV	**R (%)**	5.5%	6.0%	5.0%	6.9%	83.3%	81.7%	89.7%	91.5%
	I (%)	0.0%	0.0%	0.0%	0.0%	1.0%	0.0%	0.0%	0.0%
	S (%)	93.9%	94.0%	95.0%	93.1%	15.7%	18.3%	10.3%	8.5%
	N	*327*	*397*	*519*	*524*	*96*	*104*	*146*	*117*

R: resistant; I: intermediate; S: susceptible; N: number of strains tested

Source: SNMC. SGVRESP. ASPCAT.

Overall, the percentage of resistance to aminoglycosides was 6.9% (173/2,500) to gentamicin and 8.9% (152/1,701) to tobramycin in MSSA; and 11.8% (75/637) to gentamicin and 47.1% (250/531) to tobramycin in MRSA. There were no statistically significant variations between 2016 and 2019 in the percentage of strains resistant and susceptible to these antibiotics (Table 3).

Table 3. Evolution of antibiotic sensitivity of *Staphylococcus aureus* to aminoglycosides: gentamicin (GEN) and tobramycin (TOB). Catalonia, 2016-2019

		MSSA 2016	MSSA 2017	MSSA 2018	MSSA 2019	MRSA 2016	MRSA 2017	MRSA 2018	MRSA 2019
GEN	**R (%) #**	**9.8%**	**7.2%**	**5.8%**	**6.5%**	**12.5%**	**10.6%**	**8.6%**	**15.0%**
	I (%)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	S (%)	90.2%	92.8%	94.2%	93.5%	87.5%	89.4%	91.4%	85.0%
	N	*367*	*486*	*755*	*892*	*88*	*113*	*209*	*227*
TOB	**R (%)**	**7.4%**	**11.9%**	**8.6%**	**8.0%**	**49.0%**	**41.2%**	**51.1%**	**45.7%**
	I (%)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	S (%)	92.6%	88.1%	91.4%	92.0%	51.0%	58.8%	48.9%	54.3%
	N	*108*	*336*	*523*	*734*	*49*	*97*	*188*	*197*

R: resistant; I: intermediate; S: susceptible; N: number of strains tested
Source: SNMC. SGVRESP. ASPCAT.

Resistance to erythromycin occurred in 19.2% (485/2527) of MSSA and 56.1% (361/644) of MRSA. In MSSA, there was a 42.6% increase in 2019 compared to 2016 (p = 0.0192) in the resistant percentage and a 6.5% decrease in the susceptible percentage (p = 0.0234). In MRSA, there were no statistically significant differences between the two years (Table 4).

Clindamycin resistance occurred in 14.7% (377/2557) of MSSA and 29.4% (193/657) of MRSA. In MSSA, there was a statistically significant 5.9% decrease in the susceptible percentage in 2019 compared to 2016 (p = 0.0241) (Table 4).

Table 4. Evolution of antibiotic susceptibility of *Staphylococcus aureus* to erythromycin (ERY) and clindamycin (CLI). Catalonia, 2016-2019

		MSSA 2016	MSSA 2017	MSSA 2018	MSSA 2019	MRSA 2016	MRSA 2017	MRSA 2018	MRSA 2019
ERY	**R (%)#**	**13.6%**	**19.8%**	**21.2%**	**19.4% ***	**60.0%**	**53.4%**	**55.2%**	**57.1%**
	I (%)	0.3%	0.6%	0.1%	0.1%	0.0%	0.0%	0.0%	0.0%
	S (%)	86.1%	79.6%	78.7%	80.5% *	40.0%	46.6%	44.8%	42.9%
	N	*367*	*485*	*808*	*867*	*70*	*118*	*232*	*224*
CLI	**R (%)**	**11.2%**	**15.0%**	**16.3%**	**14.6%**	**36.6%**	**30.5%**	**26.2%**	**28.5%**
	I (%)	0.2%	1.2%	1.0%	2.0%	0%	2.5%	0.5%	0.4%
	S (%)	88.6%	83.8%	82.7%	83.4% *	63.4%	67.0%	73.3%	71.1%
	N	*367*	*486*	*809*	*895*	*101*	*118*	*210*	*228*

R: resistant; I: intermediate; S: susceptible; N: number of strains tested; * statistically significant variation 2016 - 2019.
Source: SNMC. SGVRESP. ASPCAT.

Overall, tetracycline resistance occurred in 2.7% (49/1788) of MSSA and 8.6% (41/476) of MRSA. Rifampicin resistance occurred in 0.5% (12/2,394) of MSSA and 2.2% (14/639) of MRSA. Resistance to trimethoprim/sulfamethoxazole occurred in 1.2% (31/2,544) of MSSA and 2.4% (16/675) of MRSA.

Table 5 shows the evolution of these resistances by year of study. There were no statistically significant differences in the percentage of MSSA and MRSA strains resistant and susceptible to tetracycline and trimethoprim/sulfamethoxazole.

With respect to rifampicin, there was a 91.7% decrease in the percentage of resistant MSSA in 2019 compared to 2016 ($p = 0.0468$) and an 8.3% increase in the percentage of susceptible MSSA ($p < 0.0001$). There were no significant differences in the percentage of MRSA susceptible or resistant to this antibiotic between 2016 and 2019 (Table 5).

Table 5. Evolution of antibiotic susceptibility of *Staphylococcus aureus* to tetracycline (TET), rifampicin (RIF) and trimethoprim/sulfamethoxazole (TMS). Catalonia, 2016-2019

		MSSA 2016	MSSA 2017	MSSA 2018	MSSA 2019	MRSA 2016	MRSA 2017	MRSA 2018	MRSA 2019
TET	**R (%)#**	**2.8%**	**2.5%**	**2.8%**	**2.9%**	**6.8%**	**6.8%**	**10.7%**	**9.2%**
	I (%)	0%	0%	0.2%	0.2%	0%	0%	0%	0%
	S (%)	97.2%	97.5%	97.0%	96.9%	93.2%	93.2%	89.3%	90.8%
	N	*317*	*478*	*507*	*486*	*88*	*117*	*140*	*131*
RIF	**R (%)**	**1.2%**	**0.2%**	**0.8%**	**0.1% ***	**3.2%**	**2.6%**	**1.8%**	**1.9%**
	I (%)	6.6%	0%	0.8%	0%	4.2%	0.8%	1.4%	0%
	S (%)	92.2%	99.8%	98.4%	99.9% *	92.6%	96.6%	96.8%	98.1%
	N	*346*	*467*	*755*	*826*	*95*	*117*	*216*	*211*
TMS	**R (%)**	**1.6%**	**1.9%**	**1.1%**	**0.8%**	**1.0%**	**3.4%**	**2.2%**	**2.7%**
	I (%)	0%	0%	0.1%	0.1%	0%	0.8%	0.4%	0.4%
	S (%)	98.4%	98.1%	98.8%	99.1%	99.0%	95.8%	97.4%	96.9%
	N	*367*	*477*	*808*	*892*	*100*	*118*	*230*	*227*

R: resistant; I: intermediate; S: susceptible; N: number of strains tested;
* statistically significant variation 2016 - 2019.
Source: SNMC. SGVRESP. ASPCAT.

Regarding vancomycin resistance, 1/118 (0.8%) MRSA strains were detected in 2017 and 2/808 (0.2%) MSSA strains in 2018.

In terms of daptomycin resistance, 6/2,271 (0.3%) MSSA and 4/649 (0.6%) MRSA resistant strains were isolated in the whole period.

Two MRSA strains resistant to linezolid were detected: 1/100 (1.0%) in 2016 and 1/116 (0.9%) in 2017.

Table 6 shows the evolution per study year of these antibiotics.

Table 6. Evolution of antibiotic sensitivity of *Staphylococcus aureus* to vancomycin (VAN), daptomycin (DAP) and linezolid (LNZ). Catalonia, 2016-2019

		MSSA 2016	MSSA 2017	MSSA 2018	MSSA 2019	MRSA 2016	MRSA 2017	MRSA 2018	MRSA 2019
VAN	**R (%)#**	**0.0%**	**0.0%**	**0.2%**	**0.0%**	**0.0%**	**0.8%**	**0.0%**	**0.0%**
	I (%)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	S (%)	100.0%	100.0%	99.8%	100.0%	100.0%	99.2%	100.0%	100.0%
	N	*362*	*532*	*808*	*902*	*100*	*118*	*233*	*227*
DAP	**R (%)**	**0.3%**	**0.5%**	**0.3%**	**0.1%**	**0.0%**	**3.4%**	**0.0%**	**0.0%**
	I (%)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	S (%)	99.7%	99.5%	99.7%	99.9%	100.0%	96.6%	100.0%	100.0%
	N	*329*	*477*	*717*	*794*	*99*	*117*	*212*	*221*
LNZ	**R (%)**	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**1.0%**	**0.9%**	**0.0%**	**0.0%**
	I (%)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	S (%)	100.0%	100.0%	100.0%	100.0%	99.0%	99.1%	100.0%	100.0%
	N	*361*	*517*	*796*	*881*	*100*	*116*	*231*	*222*

R: resistant; I: intermediate; S: susceptible; N: number of strains tested.
Source: SNMC. SGVRESP. ASPCAT.

No data concerning the study of the presence of the *mec*C gene were reported by any centre.

4.3 Monitoring antibiotic susceptibility and mechanisms of resistance: gram-negative bacilli

4.3.1 Enterobacteriaceae: *Escherichia coli*

The antibiotic susceptibility of *Escherichia coli* to β-lactams (ertapenem, imipenem, amoxicillin/clavulanic acid, ampicillin, cefotaxime), aminoglycosides (amikacin, gentamicin), ciprofloxacin and trimethoprim/sulfamethoxazole was tested.

Overall, very low resistance was observed for carbapenems, with 0.1% (8/9,118) being resistant to imipenem and 0.2% (20/8,653) to ertapenem. There were no statistically significant differences in the percentage of either susceptible or resistant between 2016 and 2019 (Table 7).

30.3% (2,562/8,455) of strains were resistant to amoxicillin/clavulanic acid and 65.4% (6,077/9,288) to ampicillin. 15.1% (1,347/8,941) of strains were resistant to cefotaxime. The percentage of strains resistant and susceptible to these antibiotics remained constant over time (Table 7).

Table 7. Evolution of antibiotic susceptibility of *Escherichia coli* to β-lactams. Catalonia, 2016-2019

		2016	2017	2018	2019	Variation (2016-19)
Ertapenem	**Resistant (%)**	0.1%	0.1%	0.4%	0.2%	100.0%
	Intermediate (%)	0.0%	0.1%	0.0%	0.0%	
	Susceptible (%)	99.9%	99.8%	99.6%	99.8%	-0.1%
	Total strains	1,473	1,671	2,730	2,779	
Imipenem	**Resistant (%)**	0.1%	0.1%	0.1%	0.1%	0.0%
	Intermediate (%)	0.2%	0.0%	0.1%	0.1%	
	Susceptible (%)	99.7%	99.9%	99.8%	99.8%	0.1%
	Total strains	1,648	1,885	2,812	2,773	
AMC	**Resistant (%)**	31.2%	28.3%	30.8%	30.4%	-2.5%
	Intermediate (%)	0.0%	0.0%	0.0%	0.0%	
	Susceptible (%)	68.8%	71.7%	69.2%	69.6%	1%
	Total strains	1,499	1,528	2,511	2,917	
Ampicillin	**Resistant (%)**	66.9%	66.2%	65.1%	64.4%	-3.7%
	Intermediate (%)	0.0%	0.0%	0.0%	0.0%	
	Susceptible (%)	33.1%	33.8%	34.9%	35.6%	7.5%
	Total strains	1,652	1,896	2,813	2,927	
Cefotaxime	**Resistant (%)**	15.1%	14.8%	14.8%	15.5%	2.6%
	Intermediate (%)	0.4%	0.3%	0.2%	0.1%	
	Susceptible (%)	84.5%	84.9%	85.0%	84.4%	-0.11%
	Total strains	1,643	1,571	2,795	2,932	

Source: SNMC. SGVRESP. ASPCAT. AMC: amoxicillin/clavulanic acid.

For aminoglycosides, 1.3% (120/9,138) of strains were resistant to amikacin and 13.3% (1,230/9,266) to gentamicin. There was a significant increase of 2.1% in the percentage of amikacin-susceptible strains between 2016 and 2019 (p = 0.0028) (Table 8).

Table 8. Evolution of antibiotic susceptibility of *Escherichia coli* to aminoglycosides. Catalonia, 2016-2019

		2016	2017	2018	2019	Variation (2016-19)
Amikacin	**Resistant (%)**	1.4%	1.0%	1.7%	1.1%	-21.4%
	Intermediate (%)	4.4%	5.5%	3.4%	2.7%	
	Susceptible (%)	94.2%	93.5%	94.9%	96.2%	2.1% *
	Total strains	1.601	1.857	2.756	2.924	
Gentamicin	**Resistant (%)**	13.3%	13.0%	13.1%	13.7%	3.0%
	Intermediate (%)	1.8%	1.5%	1.2%	2.1%	
	Susceptible (%)	84.9%	85.5%	85.8%	84.2%	-0.8%
	Total strains	1.649	1.899	2.801	2.917	

Source: SNMC. SGVRESP. ASPCAT. (*statistically significant)

33.9% (2,899/8,562) of strains were resistant to ciprofloxacin and 32.9% (2,927/8,891) to trimethoprim/sulfamethoxazole.

Between 2016 and 2019, there was a significant 14.2% decrease in the percentage of strains resistant to ciprofloxacin (p = 0.0002) and a significant 7.3% increase in the percentage of susceptible strains (p = 0.0062).

Regarding trimethoprim/sulfamethoxazole, between 2016 and 2019 there was a significant 10.7% decrease in the percentage of resistant strains (p = 0.0091) and a significant 5.9% increase in the percentage of susceptible strains (p = 0.0116).

Table 9. Evolution of antibiotic susceptibility of *Escherichia coli* to ciprofloxacin and trimethoprim/sulfamethoxazole (TMS). Catalonia, 2016-2019

		2016	2017	2018	2019	Variation (2016-19)
Ciprofloxacin	**Resistant (%)**	38.6%	33.0%	32.3%	33.1%	-14.2% *
	Intermediate (%)	3.7%	6.2%	3.2%	5.0%	
	Susceptible (%)	57.7%	60.8%	64.5%	61.9%	7.3% *
	Total strains	1,649	1,478	2,673	2,762	
TMS	**Resistant (%)**	36.3%	30.9%	32.8%	32.4%	-10.7% *
	Intermediate (%)	0.1%	0.4%	0.0%	0.2%	
	Susceptible (%)	63.6%	68.7%	67.2%	67.4%	5.9% *
	Total strains	1,654	1,805	2,672	2,760	

Source: SNMC. SGVRESP. ASPCAT. (*statistically significant)

Resistance mechanisms were analysed for carbapenemases (OXA-48), metallo-β-lactamases (IMP, NDM and VIM) and serine-carbapenemases (GES and KPC).

For these resistance mechanisms, 1,096 strains were tested in 2016 (except for GES, where 630 strains were tested), 1,095 strains in 2017, 1,184 strains in 2018 and 1,013 strains in 2019.

No positive strains were detected for the following resistance mechanisms: metallo-β-lactamases (IMP and VIM) and serine-carbapenemases (GES).

Resistance mechanisms were detected for carbapenemases (OXA-48), serine-carbapenemases (KPC) and metallo-β-lactamases (NDM). There was a 25% increase in the percentage of OXA-48-positive strains, albeit not statistically significant. Three KPC-positive isolates were reported: 1 (0.1%) in 2018 and 2 (0.2%) in 2019. Regarding NDM, one positive isolate was detected in 2018 (Table 10).

Table 10. *Escherichia coli* resistance mechanisms by year. Catalonia, 2016-2019

		2016	2017	2018	2019	Variation (2016 - 2019)
OXA-48	Tested (N)	1,096	1,533	1,184	1,016	
	Positive (N)	4	1	5	5	
	Positive (%)	**0.4%**	**0.1%**	**0.4%**	**0.5%**	**25.0%**
KPC	Tested (N)	1,096	1,095	1,603	1,014	
	Positive (N)	0	0	1	2	
	Positive (%)	0.0%	0.0%	**0.1%**	**0.2%**	**-**
NDM	Tested (N)	1,096	1,095	1,603	1,013	
	Positive (N)	0	0	1	0	
	Positive (%)	0.0%	0.0%	**0.1%**	0.0%	**-**

Source: SNMC. SGVRESP. ASPCAT.

In 2016, 318 strains were tested for multidrug resistance, of which 52 strains (16.4%) were found to be multidrug-resistant (MDR): 3 in carbapenemases, 45 in BLEE and 4 in plasmid AmpC.

4.3.2 Enterobacteriaceae: *Klebsiella pneumoniae*

The antibiotic susceptibility of *Klebsiella pneumoniae* to β-lactams (ertapenem, imipenem, amoxicillin/clavulanic acid, cefotaxime), aminoglycosides (amikacin, gentamicin), ciprofloxacin, and trimethoprim/sulfamethoxazole was tested.

It was found that the percentage of strains resistant to all the antibiotics was significantly higher in 2016 than in 2019. These data might reflect an outbreak of *Klebsiella pneumoniae* that took place in Catalonia in 2016 (13). Hence, the statistical study of the increase or decrease in *Klebsiella pneumoniae* resistance to antibiotics in Catalonia was performed comparing 2017 and 2019.

Overall, the percentage of strains resistant to β-lactams was 5.6% (150/2,670) for ertapenem, 1.8% (49/2,717) for imipenem, 38.2% (956/2,501) for amoxicillin/clavulanic acid and 30.5% (833/2,732) for cefotaxime. There were no statistically significant differences in the percentage of susceptible strains in 2019 compared to 2017 (Table 11).

Table 11. Evolution of antibiotic susceptibility of *Klebsiella pneumoniae* to β-lactams. Catalonia, 2016-2019

		2016	2017	2018	2019	Variation (2017-19)
Ertapenem	**Resistant (%)**	9.7%	4.8%	5.1%	4.4%	-8.3%
	Intermediate (%)	0.9%	0.4%	0.2%	0.6%	
	Susceptible (%)	89.4%	94.8%	94.7%	95.0%	0.21%
	Total strains	464	499	826	881	
Imipenem	**Resistant (%)**	2.1%	1.7%	1.9%	1.6%	-5.9%
	Intermediate (%)	1.3%	1.1%	2.2%	0.7%	
	Susceptible (%)	96.6%	97.1%	95.9%	97.7%	0.6%
	Total strains	471	523	845	878	
AMC	**Resistant (%)**	45.4%	38.8%	34.5%	38.4%	-1.0%
	Intermediate (%)	0.0%	0.0%	0.0%	0.0%	
	Susceptible (%)	54.6%	61.2%	65.5%	61.6%	0.7%
	Total strains	379	376	833	913	
Cefotaxime	**Resistant (%)**	35.4%	30.1%	28.4%	30.1%	0.0%
	Intermediate (%)	0.0%	0.2%	0.0%	0.1%	
	Susceptible (%)	64.6%	69.7%	71.6%	69.8%	0.1%
	Total strains	469	509	838	916	

Source: SNMC. SGVRESP. ASPCAT. AMC: amoxicillin/clavulanic acid.

Regarding aminoglycosides, 1.3% (37/2,742) of strains were resistant to amikacin and 16.4% (439/2,672) to gentamicin. The increase in the percentage of amikacin-susceptible strains in 2019 compared to 2017 was statistically significant (p = 0.0001) (Table 12).

Table 12. Evolution of antibiotic susceptibility of *Klebsiella pneumoniae* to aminoglycosides. Catalonia, 2016-2019

		2016	2017	2018	2019	Variation (2017-19)
Amikacin	**Resistant (%)**	2.7%	1.8%	0.6%	1.1%	-38.9%
	Intermediate (%)	9.7%	8.7%	2.5%	3.8%	
	Susceptible (%)	87.6%	89.5%	96.9%	95.1%	6.3% *
	Total strains	474	516	836	916	
Gentamicin	**Resistant (%)**	17.7%	17.0%	15.5%	16.4%	-3.5%
	Intermediate (%)	0.5%	0.2%	0.4%	0.3%	
	Susceptible (%)	81.8%	82.8%	84.2%	83.3%	0.6%
	Total strains	391	528	840	913	

Source: SNMC. SGVRESP. ASPCAT. (*statistically significant)

In the entire period analysed, 32.1% (825/2,573) of strains were resistant to ciprofloxacin and 31.3% (840/2,684) to trimethoprim/sulfamethoxazole. There were no statistically significant differences in the percentage of resistant and susceptible strains between 2017 and 2019 (Table 13).

Table 13. Evolution of antibiotic susceptibility of *Klebsiella pneumoniae* to cefotaxime, ciprofloxacin and trimethoprim/sulfamethoxazole (TMS). Catalonia, 2016-2019

		2016	2017	2018	2019	Variation (2017-19)
Ciprofloxacin	**Resistant (%)**	36.5%	31.9%	28.8%	32.8%	2.8%
	Intermediate (%)	3.0%	2.0%	2.2%	3.2%	
	Susceptible (%)	60.5%	66.1%	69.0%	64.0%	-3.2%
	Total strains	471	401	823	878	
TMS	**Resistant (%)**	35.9%	31.0%	27.4%	32.7%	5.5%
	Intermediate (%)	0.2%	1.4%	0.2%	0.6%	
	Susceptible (%)	63.9%	67.6%	72.4%	66.7%	-1.3%
	Total strains	471	513	822	878	

Source: SNMC. SGVRESP. ASPCAT.

The following resistance mechanisms were tested for: carbapenemases (OXA-48), metallo-β-lactamases (IMP, NDM and VIM) and serine-carbapenemases (GES and KPC).

No positive strains were detected for the following resistance mechanisms: metallo-β-lactamases (IMP) and serine-carbapenemases (GES). For these resistance mechanisms, 353 and 149 strains were tested in 2016 for IMP and GES, respectively; 232 strains in 2017 for each of the mechanisms; 323 and 321 strains in 2018 for IMP and GES, respectively; and 286 and 282 strains in 2019 for IMP and GES, respectively.

Resistance mechanisms were detected for carbapenemases (OXA-48), metallo-β-lactamases (NDM and VIM) and serine-carbapenemases (KPC) (Table 14).

Table 14. *Klebsiella pneumoniae* resistance mechanisms by year. Catalonia, 2016-2019

		2016	2017	2018	2019	Variation (2017 - 2019)
OXA-48	Tested (N)	419	414	486	442	
	Positive (N)	38	17	32	25	
	Positive (%)	9.1%	4.1%	6.6%	5.7%	39.0%
KPC	Tested (N)	353	414	521	441	
	Positive (N)	0	2	10	2	
	Positive (%)	0.0%	0.5%	1.9%	0.5%	0.0%
NDM	Tested (N)	356	232	323	441	
	Positive (N)	5	0	3	3	
	Positive (%)	1.4%	0.0%	0.9%	0.7%	-
VIM	Tested (N)	356	232	323	287	
	Positive (N)	1	0	1	5	
	Positive (%)	0.3%	0.0%	0.3%	1.7%	-

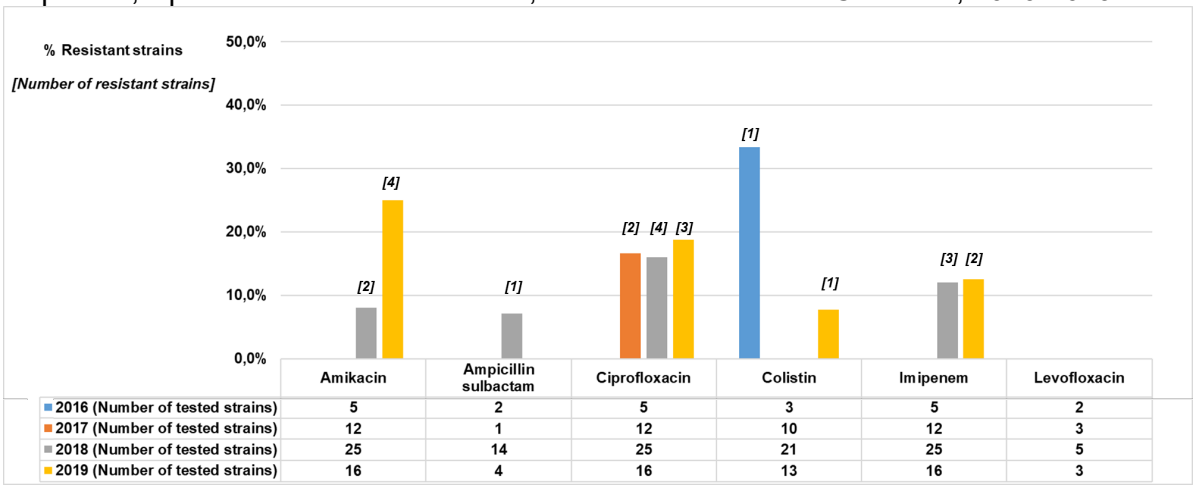
Source: SNMC. SGVRESP. ASPCAT.

In 2016, 80 strains were tested for multidrug resistance, with 29 strains (36.3%) multidrug-resistant (MDR).

4.3.3 Non-fermenters: *Acinetobacter baumannii*

Resistance of *Acinetobacter baumannii* to ampicillin sulbactam, imipenem, ciprofloxacin and levofloxacin, colistin and amikacin was tested. The results are shown in Figure 13.

Figure 13. Evolution of *Acinetobacter baumannii* strains resistant to ampicillin sulbactam, imipenem, ciprofloxacin and levofloxacin, colistin and amikacin. Catalonia, 2016-2019



Source: SNMC. SGVRESP. ASPCAT.

In the whole period, only one ampicillin sulbactam-resistant strain was reported in 2018.

Three strains resistant to imipenem were detected in 2018 and two strains in 2019.

Regarding quinolones, no strains resistant to levofloxacin were detected in the whole study period while 2 strains resistant to ciprofloxacin were isolated in 2017 and 3 strains in 2018 and 2019.

Two strains resistant to colistin were detected, 1 in 2016 and 1 in 2019.
As for amikacin resistance, 2 resistant strains were isolated in 2018 and 4 resistant strains in 2019.

Three centres provided information on the following resistance mechanisms: carbapenemases (OXA-23, OXA-40 and OXA-58) and metallo-β-lactamases (IMP, NDM and VIM). They were tested in 5 strains: 1 in 2016, 2 in 2017 and 2 in 2018. All were negative for these resistance mechanisms.

4.3.4 Non-fermenters: *Pseudomonas aeruginosa*

The susceptibility of *Pseudomonas aeruginosa* to β-lactam carbapenems (ertapenem, meropenem), aminoglycosides (amikacin, gentamicin, tobramycin), cephalosporins (cefepime, ceftazidime), quinolones (ciprofloxacin, levofloxacin) and colistin was tested.

Regarding carbapenems, 23.2% (436/1,883) of strains were resistant to imipenem and 14.7% (273/1,854) to meropenem. There were no statistically significant differences in the percentage of resistant or susceptible strains between 2016 and 2019 (Table 15).

Table 15. Evolution of antibiotic susceptibility of *Pseudomonas aeruginosa* to carbapenems. Catalonia, 2016-2019

		2016	2017	2018	2019	Variation (2016-19)
Imipenem	**Resistant (%)**	25.3%	24.2%	20.6%	23.8%	-5.9%
	Intermediate (%)	2.3%	3.5%	1.2%	0.0%	
	Susceptible (%)	72.4%	72.3%	78.2%	76.2%	5.2%
	Total strains	344	347	579	613	
Meropenem	**Resistant (%)**	16.3%	15.5%	14.2%	14.1%	-13.5%
	Intermediate (%)	11.8%	13.0%	7.5%	8.3%	
	Susceptible (%)	71.9%	71.5%	78.3%	77.6%	7.9%
	Total strains	295	323	549	687	

Source: SNMC. SGVRESP. ASPCAT.

For aminoglycosides, 3.2% (62/1,961) of strains were resistant to amikacin, 16.9% (334/1,972) to gentamicin and 12.8% (252/1,962) to tobramycin.

There were no statistically significant differences in the percentages of either resistant or susceptible strains between 2016 and 2019 for amikacin and gentamicin. Resistance to tobramycin was 33.5% lower in 2019 than in 2016 (p = 0.0197) (Table 16).

Table 16. Evolution of antibiotic susceptibility of *Pseudomonas aeruginosa* to aminoglycosides. Catalonia, 2016-2019

		2016	2017	2018	2019	Variation (2016-19)
Amikacin	**Resistant (%)**	4.4%	2.9%	3.1%	2.7%	-38.6%
	Intermediate (%)	3.0%	4.3%	2.8%	3.9%	
	Susceptible (%)	92.6%	92.8%	94.1%	93.4%	0.9%
	Total strains	337	347	581	696	
Gentamicin	**Resistant (%)**	18.0%	21.3%	14.8%	16.0%	-11.1%
	Intermediate (%)	0.0%	0.0%	0.0%	0.0%	
	Susceptible (%)	82.0%	78.7%	85.2%	84.0%	2.4%
	Total strains	344	352	581	695	
Tobramycin	**Resistant (%)**	15.8%	18.6%	10.4%	10.5%	-33.5% *
	Intermediate (%)	0.0%	0.0%	0.0%	0.0%	
	Susceptible (%)	84.2%	81.4%	89.6%	89.5%	6.3% *
	Total strains	341	350	579	692	

Source: SNMC. SGVRESP. ASPCAT. (*statistically significant)

Regarding quinolones, 25.0% (451/1,805) of strains were resistant to ciprofloxacin and 27.8% (193/693) to levofloxacin. There were no statistically significant differences in the percentage of resistant and susceptible strains between 2016 and 2019 for these antibiotics (Table 17).

Table 17. Evolution of antibiotic susceptibility of *Pseudomonas aeruginosa* to quinolones. Catalonia, 2016-2019

		2016	2017	2018	2019	Variation (2016-19)
Ciprofloxacin	**Resistant (%)**	22.4%	30.4%	22.2%	25.9%	15.6%
	Intermediate (%)	1.4%	0.0%	0.0%	0.0%	
	Susceptible (%)	76.2%	69.6%	77.8%	74.1%	-2.7%
	Total strains	344	326	514	621	
Levofloxacin	**Resistant (%)**	17.9%	32.1%	20.9%	30.5%	70.4%
	Intermediate (%)	0.0%	0.0%	0.0%	0.0%	
	Susceptible (%)	82.1%	67.9%	79.1%	69.5%	-15.3%
	Total strains	56	209	153	275	

Source: SNMC. SGVRESP. ASPCAT.

For cephalosporins, 21.0% (376/1,790) of strains were resistant to cefepime and 20.4% (384/1,878) to ceftazidime. There were no statistically significant differences in the percentage of resistant and susceptible strains between 2016 and 2019 (Table 18).

Table 18. Evolution of antibiotic susceptibility of *Pseudomonas aeruginosa* to cephalosporins. Catalonia, 2016-2019

		2016	2017	2018	2019	Variation (2016-19)
Cefepime	**Resistant (%)**	20.1%	22.3%	19.4%	22.4%	11.4%
	Intermediate (%)	0.0%	0.0%	0.0%	0.0%	
	Susceptible (%)	79.9%	77.7%	80.6%	77.6%	-2.9%
	Total strains	324	273	558	635	
Ceftazidime	**Resistant (%)**	19.5%	24.8%	17.3%	21.5%	10.3%
	Intermediate (%)	0.0%	0.0%	0.0%	0.0%	
	Susceptible (%)	80.5%	75.2%	82.7%	78.5%	2.5%
	Total strains	329	339	572	638	

Source: SNMC. SGVRESP. ASPCAT.

0.5% (9/1,749) of strains were resistant to colistin. Colistin-resistant strains were detected from 2017 onwards: 1 strain in 2017, 2 strains in 2018, and 6 strains in 2019 (Table 19).

21.8% (419/1,920) of strains were resistant to piperacillin/tazobactam. There were no statistically significant differences in the percentage of resistant and susceptible strains between 2016 and 2019 (Table 19).

Table 19. Analysis of the evolution of antibiotic susceptibility of *Pseudomonas aeruginosa* to colistin and piperacillin/tazobactam (PTZ). Catalonia, 2016-2019

		2016	2017	2018	2019	Variation (2016-19)
Colistin	**Resistant (%)**	0.0%	0.3%	0.4%	1.0%	-
	Intermediate (%)	0.0%	0.0%	0.0%	0.0%	
	Susceptible (%)	100.0%	99.7%	99.6%	99.0%	-1%
	Total strains	303	295	528	623	
PTZ	**Resistant (%)**	21.3%	24.1%	19.1%	23.3%	9.4%
	Intermediate (%)	0.0%	0.0%	0.0%	0.0%	
	Susceptible (%)	78.7%	75.9%	80.9%	76.7%	2.5%
	Total strains	329	352	581	658	

Source: SNMC. SGVRESP. ASPCAT.

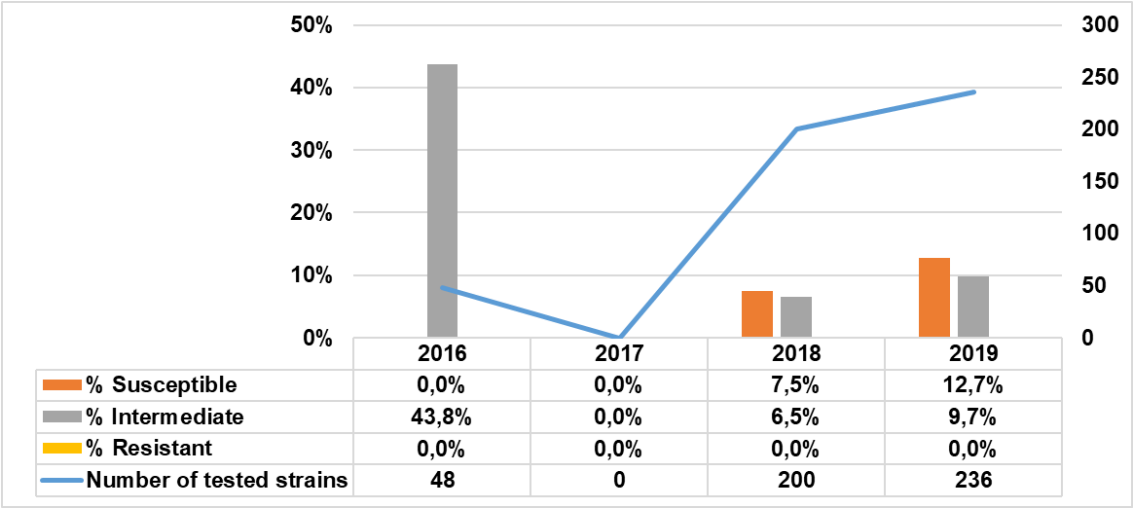
The presence of the following resistance mechanisms was monitored: carbapenemases (OXA-40 and OXA-198), metallo-β-lactamases (GIM, IMP, SPM, VIM) and serine-carbapenemases (GES and KPC).

The number of strains tested per year was 48 strains for OXA-198, OXA-40, GIM and GES, and 204 for IMP, SPM, KPC and VIM in 2016; 140 strains in 2017 except for VIM (254 strains); 132 strains in 2018 except for VIM (273 strains); and 161 strains for OXA-198, OXA-40 and GES, 191 for VIM and 202 for GIM, IMP, SPM and KPC in 2019.

The only resistance mechanism detected during the study period was metallo-β-lactamase (VIM): 3 (1.5%) positive strains in 2016, 2 (0.8%) positive strains in 2017, 6 (2.2%) positive strains in 2018 and 7 (3.7%) positive strains in 2019. There was a 149.2% non-statistically significant (p = 0.286) increase in the percentage of positive strains in 2019 compared to 2016.

Figure 14 shows the percentage of multidrug-resistant, extensively drug-resistant and pandrug-resistant strains by year. No pandrug-resistant strains were detected in the period studied. Over the period studied, there was an increase in the number of centres reporting multidrug-resistant *P. aeruginosa*. Thus, only one centre performed the multidrug-resistance study in 2016, yielding 21 out of 48 strains tested (43.8%) as extensively drug-resistant. In 2017, no centres reported performing this type of testing. In 2018, 3 centres reported these data, obtaining 15 out of 200 (7.5%) multidrug-resistant strains and 13 out of 200 (6.5%) extensively drug-resistant strains. In 2019, 6 centres reported 30 out of 236 (12.7%) multidrug-resistant strains and 23 out of 236 (9.7%) extensively drug-resistant strains. There was an increase in the percentage of both multidrug-resistant and extensively drug-resistant strains from 2018 to 2019.

Figure 14. Evolution of *Pseudomonas aeruginosa* multidrug-resistance by years of study. Catalonia, 2016-2019



	2016	2017	2018	2019
% Susceptible	0,0%	0,0%	7,5%	12,7%
% Intermediate	43,8%	0,0%	6,5%	9,7%
% Resistant	0,0%	0,0%	0,0%	0,0%
Number of tested strains	48	0	200	236

Source: SNMC. SGVRESP. ASPCAT.

5 Conclusions

- Enterobacteriaceae accounted for the highest number of isolates, followed by *P. aeruginosa* and *S. aureus*. The percentage of isolates for *S. agalactiae*, *S. pyogenes* and *A. baumannii* was less than 1% in each case.

- Regarding *E. faecalis*, more than 99% of strains were susceptible to ampicillin. Resistance to streptomycin was 28.5% overall, decreasing over the years. Resistance to gentamicin was 30.0%. No vancomycin-resistant strains were detected.

- In *E. faecium,* overall 84.9% of strains were resistant to ampicillin and 69.7% to streptomycin. Resistance to gentamicin was 27.6% and showed a significant 42.6% decrease in 2019 compared to 2016. Two vancomycin-resistant strains were detected in 2016 and 2018 (0.14% per year, VanB and VanA phenotypes, respectively).

- Regarding *S. agalactiae*, overall 27.5% of strains were resistant to clindamycin with something of an upward trend over the years. 38.3% of the strains were resistant to erythromycin and no resistance to benzylpenicillin was detected.

- For *S. pyogenes*, one clindamycin-resistant strain was detected in 2018 (2.9%). From 2018 onwards, erythromycin-resistant strains were detected: 2 (5.9%) in 2018 and 5 (9.8%) in 2019. No resistance to benzylpenicillin was detected.

- In *S. aureus*, the MRSA percentage remained stable from 2016 (21.6%) to 2019 (20.2%).

- Regarding *S. aureus* MSSA, overall 89.7% of the strains were resistant to benzylpenicillin. Resistance to erythromycin was 19.2%. Susceptibility to this antibiotic fell by 6.5% from 2016 to 2019. 14.7% of strains were resistant to clindamycin. Susceptibility to this antibiotic fell by 5.9%. 7-10% of strains were resistant to quinolones, aminoglycosides, 2.7% to tetracycline, 1.2% of strains were resistant to trimethoprim/sulfamethoxazole and ≤ 0.5% resistant to rifampicin, daptomycin and vancomycin. No linezolid-resistant strains were detected. There was an 8.3% increase in the percentage of rifampicin-susceptible MSSA between 2016 and 2019.

- Regarding *S. aureus* MRSA, all strains were resistant to benzylpenicillin, more than 80% to quinolones, 56.1% to erythromycin, 47.1% to tobramycin, 29.4% to clindamycin, and 11.8% to gentamycin. 8.6%, 2.4% and 2.2% were resistant to tetracycline, trimethoprim/sulfamethoxazole and rifampicin, respectively. Between 0.3-0.8% of strains were resistant to daptomycin, vancomycin and linezolid, all detected in 2016-2017.

- Regarding *E. coli*, 65.4% of strains were resistant to ampicillin and 33.9% to ciprofloxacin. 28-33% of strains were resistant to amoxicillin/clavulanic acid and trimethoprim/sulfamethoxazole, 10-15% to cefotaxime and gentamicin, 1.3% to amikacin, and ≤ 0.2% to carbapenems. The percentage of strains susceptible to amikacin, ciprofloxacin and trimethoprim/sulfamethoxazole increased in 2019 compared to 2016 by 2.1%, 7.3% and 5.9%, respectively.

- In terms of resistance mechanisms, a percentage of less than 0.5% of strains positive for OXA-48 was detected in *E. coli* in all years, KPC in 2018 and 2019, and NDM in 2018. No strains positive for IMP, VIM or GES were detected.

- Regarding *K. pneumoniae*, there was a higher percentage of resistance to all antibiotics in 2016. These data might reflect an outbreak which took place in Catalonia in 2016. Hence the statistical study of the increase/decrease in resistance was performed comparing data of 2017 and 2019.

- The percentages of resistant *K. pneumoniae* strains were 38.2% to amoxicillin/clavulanate, 30-32% to ciprofloxacin, trimethoprim/sulfamethoxazole and cefotaxime, 16.4% to gentamicin, 5.6% to ertapenem, 1.8% to imipenem and 1.3% to amikacin. The percentage of amikacin-susceptible strains increased significantly in 2019 (95.1%) compared to 2017 (89.5%).

- In terms of resistance mechanisms, 4.1-9.1% of strains positive for OXA-48, 0.5-1.9% of strains positive for KPC, 0.7-1.4% for NDM, and 0.3-1.7% for VIM were detected in *K. pneumoniae*. No strains positive for IMP or GES were detected.

- Regarding *A. baumannii*, one strain was resistant to ampicillin sulbactam (2018 [7.1%]), 5 to imipenem (2018 [12.0%] and 2019 [12.5%]), 8 to ciprofloxacin (2017 [16.7%], 2018 [16.0%], 2019 [18.8%]), 2 (3.6%) to colistin (2016 [33.3%] and 2019 [7.8%]) and 6 to amikacin (2018 [8.0%] and 2019 [25.0%]). None were resistant to levofloxacin.

- For *P. aeruginosa*, aminoglycosides showed 3.2% resistance to amikacin and 12-17% to gentamicin and tobramycin, 14.7% of strains were resistant to meropenem and 20-23% to imipenem and cephalosporins (cefepime and ceftazidime), while 25-28% of strains were resistant to quinolones (ciprofloxacin and levofloxacin). Nine (0.5%) strains resistant to colistin were reported. Resistance to tobramycin fell by 33.5% in 2019 compared to 2016. The only resistance mechanism detected during the study period was metallo-β-lactamase (MIV) (1.5% of positive strains in 2016 and 3.7% in 2019).

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7 Annex 1: Participating centres

Fundació Hospital Sant Joan de Déu de Martorell, Fundació Hospital de l'Esperit Sant, Hosp. Comarcal de Blanes, Hospital Clínic de Barcelona, Hospital Casa de la Maternitat, Hospital Comarcal de Móra d'Ebre, Hospital Comarcal de Sant Bernabé, Hospital Comarcal Sant Jaume de Calella, Hospital d'Olot i Comarcal de la Garrotxa, Hospital de Figueres, Hospital de la Cerdanya, Hospital de la Santa Creu i Sant Pau, Hospital de Mataró, Hospital de Palamós, Hospital de Sant Pau i Santa Tecla, Hospital del Vendrell, Hospital de Terrassa, Hospital de Viladecans, Hospital del Mar, Hospital General - Parc Sanitari de Sant Joan de Déu, Hospital General de Catalunya, Hospital General de Granollers, Hospital General de Vic, Hospital Municipal de Badalona, Hospital Sant Joan de Déu - Esplugues de Llobregat, Hospital Sant Joan de Déu de Manresa-Fundació Althaia, Centre hospitalari Manresa – Fundació Althaia, Hospital Universitari Arnau de Vilanova, Hospital Universitari Santa Maria, Hospital Universitari de Bellvitge, Hospital Universitari de Girona Dr. Josep Trueta, Hospital Universitari Germans Trias i Pujol, Hospital Universitari Joan XXIII de Tarragona, Hospital Universitari Mútua Terrassa, Hospital Universitari Sant Joan de Reus, Hospital Comarcal d'Amposta, Hospital Universitari Vall d'Hebron, Hospital Verge de la Cinta de Tortosa, Laboratori de Referència de Catalunya, SYNLAB Diagnósticos Globales, Hospital de l'Esperança.

8 Annex 2: Antibiotics and mechanisms of resistance tested

Enterococci (*E. faecalis, E. faecium)*

Antibiotics: ampicillin, gentamicin, streptomycin, vancomycin
Resistance mechanisms: Van A phenotype, Van B phenotype

Streptococci (*S. agalactiae, S. pyogenes*)

Antibiotics: benzylpenicillin, erythromycin, clindamycin
Resistance mechanisms: M genotype, iMLSB/cMLSB phenotypes

Staphylococcus aureus (MSSA, MRSA)

Antibiotics: benzylpenicillin, oxacillin, ciprofloxacin, levofloxacin, gentamicin, tobramycin, vancomycin, erythromycin, clindamycin, tetracycline, daptomycin, linezolid, rifampicin, trimethoprim/sulfamethoxazole
Resistance mechanisms: *mecC* gene (MRSA)

Enterobacteriaceae (*E. coli, K. pneumoniae)*

Antibiotics: ampicillin (only *E. coli*), amoxicillin/clavulanic acid, cefotaxime, imipenem, ertapenem, ciprofloxacin, amikacin, gentamicin, trimethoprim/sulfamethoxazole
Resistance mechanisms: carbapenemases (OXA-48), metallo-β-lactamases (VIM), metallo-β-lactamases (NDM), metallo-β-lactamases (IMP), serine-carbapenemases (KPC), serine-carbapenemases (GES)

Acinetobacter baumannii

Antibiotics: ampicillin sulbactam, imipenem, ciprofloxacin, levofloxacin, amikacin, colistin

Resistance mechanisms: carbapenemases (OXA-40), carbapenemases (OXA-58), carbapenemases (OXA-23), metallo-β-lactamases (VIM), metallo-β-lactamases (NDM), metallo-β-lactamases (IMP)

Pseudomonas aeruginosa

Antibiotics: piperacillin / tazobactam, cefepime, ceftazidime, imipenem, meropenem, ciprofloxacin, levofloxacin, amikacin, gentamicin, tobramycin, colistin

Resistance mechanisms: metallo-β-lactamases (VIM), metallo-β-lactamases (IMP), metallo-β-lactamases (SPM), metallo-β-lactamases (GIM), serine-carbapenemases (KPC), serine-carbapenemases (GES), carbapenemases (OXA-40), carbapenemases (OXA-198)