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Report National Reference Centre *Streptococcus pneumoniae* 2019

This is a report of the National Reference Centre (NRC) for invasive *Streptococcus pneumoniae* with a focus on invasive pneumococcal disease (IPD) isolates from 2019.

We performed capsular typing (Quellung reaction) to determine the serotypes of invasive *S. pneumoniae* sent to the NRC. For children less than 16 years old we determined the capsular type onto serotype level. For adults, we did subtyping of all serogroups with serotypes that are part of the current vaccines (i.e. SG6, 7, 9, 10, 11, 12, 15, 17, 18, 19, 22, 23, 33)

Data of the NRC are based on a passive laboratory-based surveillance. During the last 10 years, 121 laboratories were involved in this surveillance, with a yearly mean of 93 laboratories sending isolates to the NRC. The geographical origin of the IPD cases remained stable during this period and reflects the distribution of the population over the different regions in Belgium. (Table 1)

Table 2 shows the origin of the sampled cultures. More than 90% of pneumococci were isolated from blood cultures and 4% from cerebrospinal fluid.

Table 3 shows the age distribution of patients from whom pneumococci were isolated from one of the three major infection sites (blood, pleural fluid and cerebrospinal fluid). Among all age groups we see a stable number of isolates compared to 2018. The number of blood culture isolates with respect to the total population increased from 1477 in 2018 to 1503 in 2019. (Figure 1)

Table 4 illustrates the distribution of invasive isolates (blood, cerebrospinal fluid, pleural fluid and joint fluid) in children during the first two years of life by capsular type for the period 2014-2019. After a subsequent increase in total number of strains from 96 in 2016, to 119 in 2017 and 137 in 2018, we note a stabilization of the total number in 2019 with 142 isolates. The predominant serotypes in 2019 are 19A (40.9%), 12F (10.2%), 10A (7.3%) and 23B (6.6%). Only 0.7% of the 142 isolates belonged to serotypes included in the 10-valent conjugate vaccine. In 2019 we see a proportion of PCV13 non-PCV10 serotypes of 45.3% (62/142), which is higher compared to 2018 (46/137(33.6%)) and 2017 (22/119(18.5%)). Of the serotypes included in PCV13 and not in PCV10: an increase in serotype 19A isolates was seen in 2019 (56/142 (40.9%) compared to 2018 (37/137 (27.0%)), serotype 3 did not increase compared to 2018 and serotype 6A was not detected. Furthermore, 79 (57.7%) of the 142 isolates belong to serotypes that

were not included in PCV13. Compared to other years, more non-typable pneumococcal isolates (5/142) were detected. This will be further investigated.

Since 2018, in contrast to previous years, all strains belonging to serogroups included in the current vaccines are identified up to the serotype level. Table 5 describes in descending order of frequency the serotypes studied in 2019. Serotype distribution is determined per age group. Overall, serotype 8 is still the most important serotype responsible for 19.3% of the IPD isolates in 2019. Serotype 19A (15.6%), 3 (11.4%), 12F (9.3%) and 6C (4.3%) are the other predominant serotypes. Compared to 2018, an increase in the proportion of serotype 19A (+5.1%), serotype 8 (+2.5%) and serotype 6C (+1.7%) was noted. The proportion of serotype 3 (-1.0%) and 12F (-0.5%) remained more stable. Differences in serotype distribution are seen in the different age groups. The highest difference in serotype proportion between children and older adults (65-84 years old) was noted for serotype 19A (33% in children versus 19% in older adults), serotype 8 (6% versus 18%) and 3 (3 versus 13%). Overall, 32.3% of serotypes are included in PCV13 and 76.1% are included in PPV23.

Table 6 shows the serotypes responsible for at least 5% of the isolates of the 4 major infection sites. Serotype 8 is the predominant type (19.6%) in blood culture and pleural fluid isolates. Serotype 19A is not only very important in blood culture isolates (15.6%) but is also, as in the past, common among otitis media strains (>25%) and this year also common among cerebrospinal fluid strains (16.4%).

Table 7 illustrates the evolution of the susceptibility to the 4 antibiotics (penicillin, tetracycline, erythromycin and levofloxacin) that are systematically tested on submitted strains. From the start of the surveillance the paper disk-diffusion technique on Mueller Hinton agar with 5% horse blood has been used. After incubation for 18 hours at 36° C with 5% CO₂ the inhibition zones are measured and interpreted according to EUCAST guidelines. For the detection of resistance to penicillin, oxacillin disks with a charge of 1 µg are used. MICs were determined by using Etest (BioMérieux, France). One hundred and seventy-seven (10.8%) of the 1643 strains showed a reduced susceptibility to penicillin (MIC > 0.06mg/L), which is fully comparable to the result of 2018. Fourteen of these 177 strains had a penicillin MIC of 2 mg/L (susceptible, increased exposure (non-meningitis)/resistant (meningitis)) and none had a MIC above 2 mg/L (resistant (non-meningitis breakpoint)). Nine strains were cefotaxime susceptible, increased exposure, and one strain with MIC of 3mg/L was categorized as resistant. All other strains were tested as cefotaxime susceptible.

We note a stable situation concerning tetracycline and erythromycin non-susceptibility. We detected resistance to levofloxacin in only one strain.

Table 8 gives an overview of the resistance percentages for penicillin, erythromycin and tetracycline in the various serotypes. Reduced penicillin susceptibility is a particular problem (>=15%) for serotypes 19A, 19F, 23B, 11A, 11C and serogroup 24. Two predominant serotypes (serotype 8 and 3) remain susceptible to penicillin. Erythromycin resistance is very high (>40%) within the serotype 19F, 6C, 33F, 14 and serogroup 24.

Table 9 illustrates the resistance rates for the different infection locations. For blood, pleural fluid and cerebrospinal fluid isolates stable non-susceptibility rates are detected.

Tables

Table 1: Characteristics of the surveillance of the Belgian National Reference Centre invasive *S. pneumoniae* during the period of 2009-2019. (*taking into account mergers of laboratories)

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
number of unique IPD isolates sent to the NRC	1949	1896	1888	1776	1671	1223	1382	1343	1518	1571	1643
number of laboratories * involved in surveillance											
all	97	95	95	96	92	92	94	94	91	91	92
sending more than 5 isolates per year	84	85	81	85	81	74	79	76	76	75	70
located in Flanders	54	54	53	54	53	52	53	54	53	53	54
located in Wallonia	34	32	32	33	30	30	32	30	28	29	28
located in Brussels	9	9	10	9	9	10	9	10	10	9	10
regional distribution of all isolates based on residence of patient (percentage)											
Flanders	58.20%	59.80%	57.50%	58.10%	58.20%	55.80%	55.60%	62.20%	63.00%	63.84%	66.83%
Wallonia	27.40%	26.90%	27.30%	28.40%	28.30%	30.50%	31.50%	25.70%	25.50%	26.10%	23.31%
Brussels	14.00%	12.20%	14.70%	12.60%	12.00%	13.10%	11.60%	10.90%	11.40%	9.87%	9.31%
other/unknown	0.70%	1.10%	0.50%	0.80%	1.50%	0.70%	1.30%	1.10%	0.10%	0.19%	0.55%

Table 2: Number of *Streptococcus pneumoniae* strains received at the for the year 2019 NRC based on sample origin and sex of the patient

sex	Sample origin						total
	blood	cerebrospinal fluid	pleural fluid	joint	middle ear fluid	other	
male	811	41	7	5	25	7	896
female	680	19	9	1	17	7	733
unknown	12	1	0	0	1	0	14
total	1503	61	16	6	43	14	1643

Table 3: Number of (a) bacteremia/pleuritis and (b) meningitis cases based on origin of isolation of *S. pneumoniae* isolates sent to the National Reference Center per age group. Bacteremia/pleuritis: isolation of *S. pneumoniae* from blood culture and/or pleural fluid. Meningitis: isolation of *S. pneumoniae* from cerebrospinal fluid with or without isolation of *S. pneumoniae* from blood culture.

(a)

Age	bacteremia and pleuritis cases												
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
<6 months	25	40	38	35	35	13	16	8	10	18	18	27	21
6-11 months	43	53	66	66	49	34	48	31	34	29	39	48	56
12-23 months	68	47	73	67	63	32	28	30	39	36	47	55	52
2-4 years	114	128	138	117	177	116	86	48	36	34	58	46	52
5-9 years	51	33	62	52	70	47	49	26	18	25	10	12	13
10-15 years	19	15	20	19	16	16	18	9	9	10	10	13	8
16-49 years	278	276	395	296	308	287	263	186	200	187	177	238	211
50-64 years	277	307	355	340	325	357	352	230	278	284	302	299	319
65-84 years	477	570	539	598	559	540	562	410	470	423	531	534	546
≥ 85 years	148	187	163	204	175	212	174	180	190	208	232	217	239
unknown	4	9	5	3	2	14	4	2	3	14	5	1	0
Total	1504	1665	1854	1797	1779	1668	1600	1160	1287	1268	1429	1490	1517

(b)

Age	meningitis cases												
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
<6 months	8	12	7	7	7	6	1	5	8	7	7	2	5
6-11 months	5	8	9	8	5	4	1	1	5	5	3	4	5
12-23 months	4	5	3	2	3	1	0	1	4	0	1	0	1
2-4 years	4	1	2	3	0	3	1	1	1	1	3	1	1
5-9 years	1	1	3	1	5	2	1	2	5	0	2	0	3
10-15 years	2	3	3	0	4	1	2	0	3	0	1	1	1
16-49 years	17	19	13	13	10	12	13	7	9	14	11	13	12
50-64 years	17	6	19	22	16	25	12	12	21	20	8	23	15
65-84 years	16	8	10	14	20	25	9	4	15	16	14	17	15
≥ 85 years	3	4	1	2	1	1	0	1	1	0	2	1	3
unknown	0	1	0	0	0	0	0	0	2	0	0	0	0
Total	77	68	70	72	71	80	40	34	74	63	52	62	61

Table 4: Serotypes causing IPD in children <2 years old for period 2014-2019 (based on isolations of *S. pneumoniae* from blood, cerebrospinal fluid, pleural fluid and joint fluid).

Serotype	2014		2015		2016		2017		2018		2019	
	Number	%	Number	%	Number	%	Number	%	Number	%	Number	%
TOTAL	79		101		96		119		137		142	
PCV7	2	2.5	2	2.0	4	4.2	4	3.4	2	1.5	1	0.7
4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
6B	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
9V	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
14	0	0.0	1	1.0	1	1.0	1	0.8	0	0.0	0	0.0
18C	1	1.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
19F	1	1.3	1	1.0	3	3.1	2	1.7	1	0.7	1	0.7
23F	0	0.0	0	0.0	0	0.0	1	0.8	1	0.7	0	0.0
PCV10 non-PCV7	1	1.3	0	0.0	3	3.1	0	0.0	1	0.7	0	0.0
1	1	1.3	0	0.0	3	3.1	0	0.0	0	0.0	0	0.0
5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
7F	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
PCV13 non-PCV10	6	7.6	4	4.0	6	6.3	22	18.5	46	33.6	62	45.3
3	2	2.5	2	2.0	4	4.2	5	4.2	9	6.6	6	4.4
6A	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
19A	4	5.1	2	2.0	2	2.1	17	14.3	37	27.0	56	40.9
Other	70	88.6	95	94.1	83	86.5	93	78.2	88	64.2	79	57.7
2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
6C	1	1.3	0	0.0	1	1.0	2	1.7	1	0.7	3	2.2
7B	0	0.0	0	0.0	0	0.0	0	0.0	2	1.5	0	0.0
7C	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0	2	1.5
8	2	2.5	1	1.0	3	3.1	1	0.8	1	0.7	5	3.6
9	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0
9L	0	0.0	0	0.0	0	0.0	1	0.8	0	0.0	1	0.7
9N	2	2.5	1	1.0	3	3.1	3	2.5	2	1.5	1	0.7
10A	10	12.7	16	15.8	9	9.4	10	8.4	6	4.4	10	7.3
10B	3	3.8	1	1.0	0	0.0	1	0.8	1	0.7	0	0.0
11A	1	1.3	2	2.0	3	3.1	1	0.8	1	0.7	1	0.7
12	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
12A	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0	0	0.0
12B	0	0.0	0	0.0	1	1.0	1	0.8	0	0.0	0	0.0
12F	18	22.8	21	20.8	10	10.4	18	15.1	12	8.8	14	10.2
13	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
15	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0
15A	2	2.5	4	4.0	3	3.1	0	0.0	4	2.9	3	2.2
15C	3	3.8	5	5.0	1	1.0	4	3.4	1	0.7	1	0.7

15F	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
15B	5	6.3	1	1.0	4	4.2	2	1.7	2	1.5	3	2.2
16	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
16F	0	0.0	2	2.0	3	3.1	0	0.0	4	2.9	0	0.0
17F	1	1.3	0	0.0	1	1.0	1	0.8	0	0.0	0	0.0
18A	0	0.0	1	1.0	0	0.0	0	0.0	1	0.7	0	0.0
19B	0	0.0	0	0.0	0	0.0	1	0.8	0	0.0	0	0.0
19C	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0
20	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0	0	0.0
21	0	0.0	1	1.0	0	0.0	1	0.8	1	0.7	0	0.0
22	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
22A	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
22F	6	7.6	2	2.0	3	3.1	2	1.7	2	1.5	3	2.2
23A	0	0.0	1	1.0	0	0.0	3	2.5	4	2.9	0	0.0
23B	1	1.3	4	4.0	3	3.1	7	5.9	5	3.6	9	6.6
24	0	0.0	0	0.0	1	1.0	0	0.0	1	0.7	3	2.2
24A	1	1.3	1	1.0	4	4.2	3	2.5	4	2.9	1	0.7
24B	0	0.0	1	1.0	4	4.2	5	4.2	3	2.2	0	0.0
24F	3	3.8	5	5.0	4	4.2	9	7.6	12	8.8	4	2.9
27	0	0.0	1	1.0	1	1.0	1	0.8	2	1.5	1	0.7
28	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
29	0	0.0	0	0.0	1	1.0	0	0.0	1	0.7	1	0.7
31	0	0.0	1	1.0	1	1.0	0	0.0	0	0.0	0	0.0
33	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
33A	1	1.3	0	0.0	0	0.0	1	0.8	1	0.7	2	1.5
33F	7	8.9	9	8.9	9	9.4	12	10.1	6	4.4	2	1.5
34	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0
35	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0
35B	2	2.5	2	2.0	2	2.1	1	0.8	3	2.2	1	0.7
35F	0	0.0	2	2.0	1	1.0	0	0.0	0	0.0	0	0.0
38	1	1.3	7	6.9	2	2.1	2	1.7	1	0.7	3	2.2
39	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
40	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Non typable	0	0.0	0	0.0	0	0.0	0	0.0	2	1.5	5	3.6

Table 5: Distribution of serotypes of IPD isolates from 2019 (n=1592) per age group (*PCV7 serotypes, ** PCV10 serotype, *** PCV13 serotype, ° PPV23 serotype, ° serotypes not included in PCV13 or PPV23)

serotype	<16 years (n=223)	16-49 years (n=225)	50-64 years (n=336)	65-84 years (n=565)	>85 years (n=243)	TOTAL (n=1592)
8 [°]	6%	36%	24%	18%	12%	19.3%
19A ^{***}	33%	8%	13%	14%	13%	15.6%
3 ^{***}	3%	8%	13%	13%	15%	11.4%
12F [°]	14%	12%	10%	7%	5%	9.3%
6C	2%	2%	3%	6%	7%	4.3%
22F [°]	1%	3%	4%	5%	5%	3.7%
23B	6%	2%	3%	3%	3%	3.2%
9N [°]	1%	5%	3%	3%	3%	3.0%
15A	2%	1%	1%	3%	4%	2.4%
10A [°]	5%	2%	2%	1%	2%	2.3%
33F [°]	2%	3%	1%	2%	4%	1.9%
11A [°]	1%	4%	1%	2%	2%	1.8%
19F [*]	1%	1%	1%	2%	2%	1.6%
14 [*]	0%	2%	3%	1%	1%	1.5%
16	0%	0%	1%	2%	2%	1.4%
24	1%	0%	2%	2%	1%	1.4%
23A	0%	1%	2%	2%	2%	1.4%
17F [°]	0%	1%	1%	1%	2%	1.0%
35B	0%	1%	1%	1%	1%	0.9%
7F ^{**}	0%	1%	0%	1%	1%	0.9%
15B [°]	2%	0%	1%	1%	1%	0.9%
38	1%	0%	0%	1%	1%	0.8%
7C	1%	0%	1%	1%	1%	0.7%
9L	0%	0%	1%	1%	1%	0.7%
non typable	2%	0%	0%	1%	0%	0.7%
31	0%	0%	0%	1%	2%	0.6%
24F	4%	0%	0%	0%	0%	0.6%
16F	0%	0%	1%	0%	1%	0.6%
20 [°]	0%	0%	1%	0%	1%	0.6%
35F	0%	0%	1%	1%	1%	0.5%
12B	0%	0%	0%	1%	1%	0.4%
15C	1%	1%	1%	0%	0%	0.4%
4 [*]	0%	1%	0%	0%	1%	0.4%
34	1%	0%	0%	0%	0%	0.3%
35	0%	0%	0%	1%	0%	0.3%

18C*	0%	0%	0%	0%	0%	0.3%
21	0%	0%	0%	0%	0%	0.2%
11C	0%	0%	1%	0%	0%	0.2%
33A	1%	0%	0%	0%	0%	0.2%
7B	0%	0%	1%	0%	0%	0.2%
6D	0%	0%	0%	0%	0%	0.2%
6A***	0%	0%	0%	0%	1%	0.2%
9V*	0%	0%	0%	0%	0%	0.2%
10B	0%	0%	0%	0%	0%	0.1%
24A	1%	0%	0%	0%	0%	0.1%
24B	0%	0%	0%	0%	0%	0.1%
1**	0%	0%	0%	0%	0%	0.1%
6B*	0%	0%	0%	0%	1%	0.1%
2"	0%	0%	0%	0%	0%	0.1%
12	0%	0%	0%	0%	0%	0.1%
13	0%	0%	0%	0%	0%	0.1%
18	0%	0%	0%	0%	0%	0.1%
19	0%	0%	0%	0%	0%	0.1%
27	0%	0%	0%	0%	0%	0.1%
29	0%	0%	0%	0%	0%	0.1%
11F	0%	0%	0%	0%	0%	0.1%
12A	0%	0%	0%	0%	0%	0.1%
14	0%	0%	0%	0%	0%	0.1%
18A	0%	0%	0%	0%	0%	0.1%
23B	0%	0%	0%	0%	0%	0.1%
48	0%	0%	0%	0%	0%	0.1%
23F*	0%	0%	0%	0%	0%	0.1%
*PCV7 serotypes	1.8%	4.9%	3.9%	4.2%	5.8%	4.1%
**PCV10 non-PCV7 serotypes	0.9%	0.9%	0.6%	1.2%	1.2%	1.0%
***PCV13 non-PCV10 serotypes	36.3%	16.0%	26.2%	27.6%	29.2%	27.1%
PCV13 serotypes	39.0%	21.8%	30.7%	33.1%	36.2%	32.3%
"PPV23 only serotypes	33.6%	66.7%	47.0%	40.4%	36.6%	44.0%
PPV23 serotypes	72.6%	88.4%	77.7%	73.3%	72.0%	76.1%

Table 6: Dominant serotypes/serogroups (>5%) for different infection localizations

blood and/or pleural fluid (n=1517)			cerebrospinal fluid (n=61)			middle ear fluid (n=43)		
serotype	number	percentage	serotype	number	percentage	serotype	number	percentage
8	297	19.6%	8	10	16.4%	19A	19	44.2%
19A	236	15.6%	19A	10	16.4%	3	5	11.6%
3	173	11.4%	3	8	13.1%	15B	4	9.3%
12F	141	9.3%	12F	7	11.5%	12F	2	4.7%
			6C	5	8.2%	19F	2	4.7%
						23B	2	4.7%
						6C	2	4.7%

Table 7: Evolution of pneumococcal antibiotic non-susceptibility (1987-2019) based on susceptibility testing of all pneumococcal strains received at the National Reference Centre (IPD strains plus strains from patients with otitis media)

	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997
	N=433	N=382	N=520	N=540	N=536	N=552	N=641	N=751	N=992	N=1289	N=1241
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
Penicilline G*	12 (2.7)	5(1.3)	15(2.8)	22(4.1)	17(3.2)	22(4.0)	15(2.3)	57(7.6)	70(7.1)	122 (9.5)	124(10)
Tetracycline	73(16.8)	40(10.4)	87(16.7)	92(17.0)	77(14.4)	85(15.4)	81(12.6)	112(14.9)	157(15.8)	237 (18.4)	288(23.2)
Ofloxacin/Levofloxacin	-	-	-	-	-	-	-	-	4(0.4)	0	3(0.2)
Erythromycin	36(8.3)	44(11.5)	64(12.3)	92(17.0)	84(15.7)	106(19.2)	138(21.5)	171(22.9)	239(24.1)	334 (25.9)	355(28.6)

* strains with MIC penicilline > 0.06 mg/L

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
	N=1205	N=1216	N=1218	N=1427	N=1542	N=1917	N=1744	N= 1737	N=1609	N=1726	N=1870	N=2044
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
171(14.2)	202(16.5)	215(17.6)	214(15)	234(15.1)	249(13)	202(11.6)	226(13)	169 (10.5)	172(10)	172 (9.2)	152 (7.4)	
338(28.0)	359(29.4)	386(31.7)	431(30.2)	474(30.7)	580(30.2)	501(28.7)	443(25.5)	443 (27.5)	398(23.1)	449 (24.0)	502 (24.5)	
2(0.1)	6(0.5)	4(0.3)	2(0.1)	7(0.5)	10(0.5)	11(0.6)	17(1)	10 (0.6)	9(0.5)	5 (0.3)	4 (0.2)	
374(31.0)	425(34.8)	445(36.5)	523(36.6)	557(36.1)	692(36.1)	618(35.4)	554(31.9)	508 (31.6)	449(26)	477 (25.5)	496 (24.3)	

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
	N=1992	N=1998	N=1841	N=1729	N=1269	N=1445	N=1384	N=1544	N=1614	N=1643
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
194(9.7)	235 (11.8)	197 (10.1)	187 (10.8)	127 (10)	163 (11.3)	135 (9.7)	172 (11.1)	176 (10.9)	177 (10.8)	
512(25.7)	552 (27.6)	533 (28.9)	412 (23.8)	230 (18.1)	241 (16.7)	190 (13.7)	221 (14.3)	269 (16.7)	285 (17.4)	
7(0.3)	7 (0.3)	7 (0.4)	9 (0.5)	1 (0.08)	2 (0.1)	3 (0.2)	1 (0.06)	2 (0.1)	1 (0.06)	
509(25.5)	537 (26.9)	476 (25.8)	417 (24.1)	229 (18)	276 (19.1)	227 (16.4)	250 (16.2)	269(16.7%)	284 (17.3)	

Table 8: Antibiotic non-susceptibility for penicillin, erythromycine and tetracyclin per serotype/serogroup for all IPD isolates sent to the National Reference Centre in 2019. *For penicillin non-susceptibility is defined by MIC penicillin > 0.06 mg/L.

Serotype	Total number of strains	penicillin*	erythromycine	tetracyclin
		% non-susceptible	% non-susceptible	% non-susceptible
1	2	0%	0%	0%
2	2	0%	0%	0%
3	181	1%	6%	8%
4	6	0%	0%	17%
8	308	0%	1%	1%
12	1	0%	0%	0%
13	1	0%	100%	0%
14	24	38%	63%	0%
16	22	0%	5%	9%
18	1	0%	0%	0%
19	1	0%	100%	100%
20	9	0%	0%	0%
21	3	0%	0%	0%
24	22	82%	82%	68%
27	1	0%	0%	0%
29	1	0%	0%	0%
31	10	0%	20%	20%
34	5	0%	20%	20%
35	4	0%	0%	0%
38	12	0%	0%	8%
10A	37	0%	3%	5%
10B	2	0%	0%	50%
11A	29	69%	0%	0%
11C	3	100%	33%	0%
11F	1	0%	100%	100%
12A	1	0%	0%	0%
12B	7	0%	0%	29%
12F	148	0%	5%	23%
15A	39	13%	33%	38%
15B	14	0%	21%	21%
15C	7	0%	14%	14%
16F	9	0%	0%	0%
17F	16	0%	0%	0%
18A	1	0%	0%	0%
18C	4	0%	0%	0%
19A	248	15%	25%	26%
19F	26	23%	73%	31%

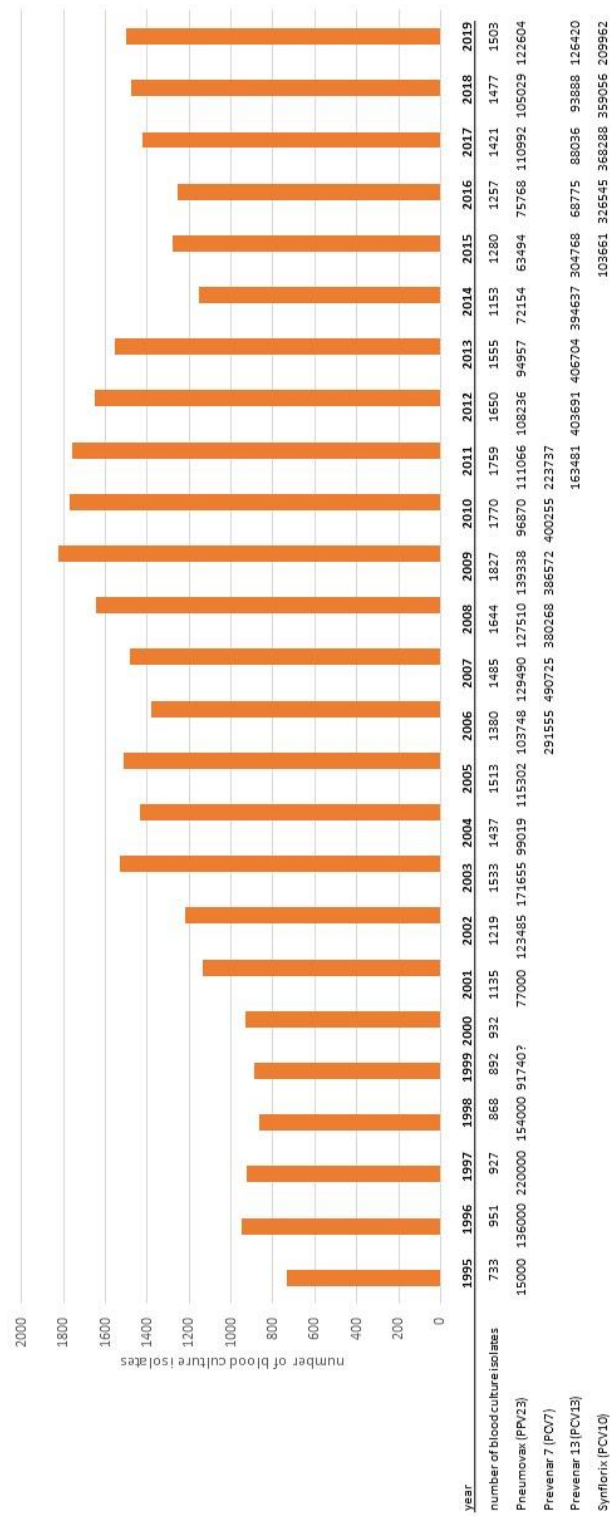
22F	59	0%	3%	3%
23A	22	5%	9%	9%
23B	51	47%	0%	0%
23F	1	0%	0%	0%
24A	2	50%	50%	50%
24B	2	100%	50%	50%
24F	10	100%	90%	90%
33A	3	0%	67%	67%
33F	31	0%	68%	39%
35B	15	20%	27%	13%
35F	8	0%	0%	0%
6A	3	33%	33%	33%
6B	2	0%	0%	50%
6C	69	6%	64%	62%
7B	3	0%	0%	0%
7C	11	0%	0%	0%
7F	14	0%	7%	14%
9L	11	0%	0%	9%
9N	47	2%	4%	9%
9V	3	67%	33%	33%
non-typable	11	64%	64%	55%
14	1	0%	100%	0%
6D	3	33%	67%	67%
23B	1	0%	0%	0%
48	1	0%	0%	0%
TOTAL	1592	10%	16%	17%

Table 9: Evolution of pneumococcal antibiotic resistance per infection localisation (1999-2019) based on susceptibility testing of all pneumococcal strains received at the National Reference Centre (IPD strains).

*For penicillin non-susceptibility is defined by MIC penicillin > 0,06 mg/L.

		% strains non-susceptible		
		penicilline G*	tetracycline	erythromycin
	1999	14.7	27.6	31.8
	2000	15.2	29.9	33.8
	2001	12.9	28.9	34.3
	2002	13.9	30.5	33.8
	2003	11.9	28.9	34
	2004	9.8	27.8	32.9
	2005	11.6	25.1	31.2
	2006	9.6	27.4	31.4
	2007	9.3	22.2	25.3
	2008	8.6	23.2	24.1
Blood + pleura	2009	6.5	23.4	23
	2010	8.7	25.7	24.8
	2011	10.3	27.3	26.12
	2012	9.6	28.8	25.4
	2013	10	24	24
	2014	9.4	17.9	17.5
	2015	10.9	17.6	18.7
	2016	9.9	13.5	15.0
	2017	10.5	14.3	15.4
	2018	10.6	16.2	16.2
	2019	9.9	16.5	16.5
	1999	7.6	16.7	24.2
	2000	22.2	31.5	42.6
	2001	6.5	28.3	39.1
	2002	8	24	38.7
	2003	8.8	28.6	31.9
	2004	12.1	33.3	42.4
	2005	14.9	25.7	33.8
	2006	13.3	16.9	27.7
	2007	10.7	16	21.3
	2008	8.8	22.1	30.9
cerobrospinal fluid	2009	12.8	34.3	31.4
	2010	15.3	27.8	30.6
	2011	20	24.3	27.1
	2012	13.6	22.2	20.9
	2013	17.5	12.5	20
	2014	5.4	17.6	14.3
	2015	10.8	14.9	18.9
	2016	7.8	9.3	12.3
	2017	8	14	24
	2018	1.6	12.9	12.9
	2019	4.9	14.8	11.7

Figure 1: Evolution of the number of blood culture isolates received at the NRC and the number of the different vaccines sold in Belgium for period 1995-2019.



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