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Date: May 2019

Report National Reference Centre *Streptococcus pneumoniae* 2018

This is a report of the National Reference Centre (NRC) for invasive *Streptococcus pneumoniae* with a focus on invasive pneumococcal disease (IPD) isolates from 2018.

We performed capsular typing (Quellung reaction) and determined the serogroups (SGT) of all invasive *S. pneumoniae* sent to the NRC. For children less than 16 years old we determined the capsular type onto serotype (STT) level. For adults, we did subtyping of all serogroups with serotypes included in 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 95 laboratories sending isolates to the NRC. The geographical origin of the IPD cases is 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 cultures and the distribution according to the sex of the patients. 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 young children under the age of 2 we see a clear increase in the number of blood culture isolates from 104 in 2017 to 130 in 2018. The number of blood culture isolates in the total population also increased from 1421 in 2017 to 1477 in 2018. (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 2013-2018. First of all we note a clear increase of the number of strains: 96 in 2016, 119 in 2017 and 137 in 2018. Only 1.5% and 2.2% of the 137 isolates belonged to capsular types (SGT/ STT) included in the 7- valent and 10- valent conjugate vaccines respectively. In 2016, 2017 and 2018 respectively 6, 22 and 46 isolates belonged to SGT/STTs that were included in the 13-valent vaccine but not in other conjugate vaccines. 37 (80.4%) of these 46 strains belong to STT 19A. Also for STT 3 we observe a (slight) increase while STT 6A was not isolated. 88 (62.4%) of the 137 isolates belong to SGT/STTs that were not included in conjugated vaccines. As in previous years the other predominant STTs are 12F, 24F, 33F and 10A.

Table 5 describes in descending order of frequency the SGT/STTS studied in 2018. There are some notable shifts compared to 2017. In 2017 SGT 12 was the most important, but in 2018 we found this type only in the fourth place. STT 8 on the other hand became the most important and responsible for 16.8% of the IPD isolates in 2018. SGT 19 (13.6 %) and STT3 (12.4%) remain frequent as in 2017. For the other SGT/STT the ranking remained stable. 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 5b) The 214 strains of SGT 19 belong mainly to STT 19A (77.6%) and to a lesser extent to STT 19F (22.4%). All SGT 22 strains belong to STT 22F. SGT 23 strains are evenly distributed between STT 23A and 23 B, with a small fraction 23F. Most of the SGT 15 isolates belong to STT 15A (73%)

Table 6 shows the SGT/STTs responsible for at least 5% of the isolates of the 4 major infection sites. SGT 8 is the predominant type (as expected) in blood culture and pleural fluid isolates. STT 19 A is not only very important in blood culture isolates but is also, as in the past, very common among otitis media strains (>25%) . Probably this high percentage of 19A is influenced by the fact that 19A isolates are more frequently resistant to antibiotics and paracentesis is more frequently performed in case of therapy-resistant otitis media

Table 7 illustrates the evolution of the susceptibility to the 4 antibiotics 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. One hundred and seventy-six (10.9%) of the 1614 strains showed a reduced susceptibility to penicillin, which is fully comparable to the result of 2017. Eight of these 176 strains had a penicillin MIC higher than 1 mg/L and only one strain had a MIC above 2 mg/L (resistance breakpoint non-meningitis EUCAST) namely 3 mg/L. This latter strain was also the only strain with a MIC higher than 2 mg/L for cefotaxime (namely 4 mg/L) which is interpreted as resistant following EUCAST guidelines. All other strains were cefotaxime susceptible, except for three strains intermediate susceptible based on EUCAST breakpoints.

For tetracycline we again find a slight increase in the proportion of non-susceptibility from 14.3% in 2017 to 16.7% in 2018. For erythromycin we note a stable situation. We found resistance to levofloxacin in only 2 strains

Table 8 gives an overview of the resistance percentages for penicillin, erythromycin and tetracycline in the various SGT/STTs. Reduced penicillin susceptibility is a particular problem (>15%) for GST/STTs: 19A, 19F, 23B, 24, 24A, 24F, 11A and 14. The two most frequent SGTs (8 and 3) remain susceptible to penicillin. Erythromycin resistance is very high (>40%) within the SGT/STTs: 19F, 24, 6C, 33F, 14, 24A and 24F. In the latter STT we see a further increase compared to 2017, also the degree of tetracycline (65%) and penicillin resistance (71%) is very high.

Table 9 illustrates the resistance rates for the different infection locations. As in previous years the otitis strains are significantly more resistant to penicillin, tetracycline and erythromycin than strains from blood cultures and cerebrospinal fluid. An explanation for this phenomenon may be that mainly otitis strains were isolated from pus after paracentesis after therapy failure. Type 19A isolates which are frequently resistant represent a high proportion of otitis isolates.

Tables

Table 1: Characteristics of the surveillance of the Belgian National Reference Centre invasive *S. pneumoniae* during period of 2007-2018. (*taking into account mergers of laboratories)

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	mean 2007-2018
number of unique IPD isolates sent to the NRC	1598	1768	1949	1896	1888	1776	1671	1223	1382	1343	1518	1571	1632
number of laboratories* involved in surveillance													
all	98	99	97	95	95	96	92	92	94	94	91	91	95
sending more than 5 isolates per year	76	83	84	85	81	85	81	74	79	76	76	75	80
located in Flanders	55	57	54	54	53	54	53	52	53	54	53	53	54
located in Wallonia	33	31	34	32	32	33	30	30	32	30	28	29	31
located in Brussels	10	11	9	9	10	9	9	10	9	10	10	9	10
regional distribution of all isolates based on residence of patient (percentage)													
Flanders	58,70%	56,10%	58,20%	59,80%	57,50%	58,10%	58,20%	55,80%	55,60%	62,20%	63,00%	63,84%	58,92%
Wallonia	26,20%	27,90%	27,10%	26,90%	27,30%	28,40%	28,30%	30,50%	31,50%	25,70%	25,50%	26,10%	27,62%
Brussels	14,50%	15,70%	14,00%	12,20%	14,70%	12,60%	12,00%	13,10%	11,60%	10,90%	11,40%	9,87%	12,71%
other/unknown	0,70%	0,40%	0,70%	1,10%	0,50%	0,80%	1,50%	0,70%	1,30%	1,10%	0,10%	0,19%	0,76%

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

	blood	cerebrospinal fluid	pleural fluid	joint	middle ear fluid	other	total
male	808	33	11	1	18	10	881
unknown	10	1	0	0	0	0	11
female	659	28	5	6	21	3	722
total	1477	62	16	7	39	13	1614

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

(b)

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

Table 4: Serotypes causing IPD in children <2 years old for period 2013-2018 (based on isolations of *S. pneumoniae* from blood, cerebrospinal fluid, pleural fluid and joint fluid). Remark: This table replaces all results from children <2 years old from previous reports.

Serotype	2013		2014		2015		2016		2017		2018	
	Number	%	Number	%	Number	%	Number	%	Number	%	Number	%
TOTAL	95		79		101		96		119		137	
PCV7	1	1.1	2	2.5	2	2.0	4	4.2	4	3.4	2	1.5
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	0	0.0	1	1.0	1	1.0	1	0.8	0	0.0
18C	0	0.0	1	1.3	0	0.0	0	0.0	0	0.0	0	0.0
19F	1	1.1	1	1.3	1	1.0	3	3.1	2	1.7	1	0.7
23F	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8	1	0.7
PCV10 non-PCV7	6	6.3	1	1.3	0	0.0	3	3.1	0	0.0	1	0.7
1	1	1.1	1	1.3	0	0.0	3	3.1	0	0.0	0	0.0
5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7
7F	5	5.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
PCV13 non-PCV10	8	8.4	6	7.6	4	4.0	6	6.3	22	18.5	46	33.6
3	2	2.1	2	2.5	2	2.0	4	4.2	5	4.2	9	6.6
6A	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
19A	6	6.3	4	5.1	2	2.0	2	2.1	17	14.3	37	27.0
other	80	84.2	70	88.6	95	94.1	83	86.5	93	78.2	88	64.2
2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
6C	0	0.0	1	1.3	0	0.0	1	1.0	2	1.7	1	0.7
7B	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	1.5
7C	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0
8	0	0.0	2	2.5	1	1.0	3	3.1	1	0.8	1	0.7
9	0	0.0	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0
9L	1	1.1	0	0.0	0	0.0	0	0.0	1	0.8	0	0.0
9N	2	2.1	2	2.5	1	1.0	3	3.1	3	2.5	2	1.5
10A	8	8.4	10	12.7	16	15.8	9	9.4	10	8.4	6	4.4
10B	0	0.0	3	3.8	1	1.0	0	0.0	1	0.8	1	0.7
11A	0	0.0	1	1.3	2	2.0	3	3.1	1	0.8	1	0.7
12	1	1.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
12A	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0
12B	0	0.0	0	0.0	0	0.0	1	1.0	1	0.8	0	0.0
12F	10	10.5	18	22.8	21	20.8	10	10.4	18	15.1	12	8.8
13	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7
15	0	0.0	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0
15A	3	3.2	2	2.5	4	4.0	3	3.1	0	0.0	4	2.9
15C	6	6.3	3	3.8	5	5.0	1	1.0	4	3.4	1	0.7
15F	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

15B	3	3.2	5	6.3	1	1.0	4	4.2	2	1.7	2	1.5
16	1	1.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
16F	0	0.0	0	0.0	2	2.0	3	3.1	0	0.0	4	2.9
17F	1	1.1	1	1.3	0	0.0	1	1.0	1	0.8	0	0.0
18A	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0	1	0.7
19B	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8	0	0.0
19C	0	0.0	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0
20	1	1.1	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0
21	1	1.1	0	0.0	1	1.0	0	0.0	1	0.8	1	0.7
22	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7
22A	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
22F	3	3.2	6	7.6	2	2.0	3	3.1	2	1.7	2	1.5
23A	3	3.2	0	0.0	1	1.0	0	0.0	3	2.5	4	2.9
23B	3	3.2	1	1.3	4	4.0	3	3.1	7	5.9	5	3.6
24	0	0.0	0	0.0	0	0.0	1	1.0	0	0.0	1	0.7
24A	0	0.0	1	1.3	1	1.0	4	4.2	3	2.5	4	2.9
24B	1	1.1	0	0.0	1	1.0	4	4.2	5	4.2	3	2.2
24F	12	12.6	3	3.8	5	5.0	4	4.2	9	7.6	12	8.8
27	1	1.1	0	0.0	1	1.0	1	1.0	1	0.8	2	1.5
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	0	0.0	1	1.0	0	0.0	1	0.7
31	0	0.0	0	0.0	1	1.0	1	1.0	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	0	0.0	1	1.3	0	0.0	0	0.0	1	0.8	1	0.7
33F	12	12.6	7	8.9	9	8.9	9	9.4	12	10.1	6	4.4
34	0	0.0	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0
35	0	0.0	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0
35B	1	1.1	2	2.5	2	2.0	2	2.1	1	0.8	3	2.2
35F	0	0.0	0	0.0	2	2.0	1	1.0	0	0.0	0	0.0
38	4	4.2	1	1.3	7	6.9	2	2.1	2	1.7	1	0.7
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	2	2.1	0	0.0	0	0.0	0	0.0	0	0.0	2	1.5

Table 5: Distribution of serogroups (a) and serotypes (b) of IPD isolates from 2018 (n=1571) (*PCV7 serotypes, ** PCV10 serotype, *** PCV13 serotype, “ PPV23 serotype)

a)

Serogroup	Number of isolates	percentage
8	264	16.8%
19	214	13.6%
3	195	12.4%
12	139	8.8%
23	92	5.9%
9	80	5.1%
24	73	4.6%
15	64	4.1%
22	58	3.7%
10	50	3.2%
6	43	2.7%
33	38	2.4%
7	36	2.3%
35	31	2.0%
11	26	1.7%
16	23	1.5%
20	19	1.2%
14	18	1.1%
17	17	1.1%
31	17	1.1%
34	15	1.0%
38	13	0.8%
1	9	0.6%
18	7	0.4%
4	6	0.4%
21	6	0.4%
13	3	0.2%
29	3	0.2%
5	2	0.1%
27	2	0.1%
32	1	0.1%
non typable	7	0.4%
TOTAL	1571	100%

b)

Serotype/Serogroup	Number of isolates	percentage
8"	264	16.8%
3***	196	12.5%
19A***	166	10.6%
12F"	137	8.7%
9N"	62	3.9%
22F"	58	3.7%
19F*	48	3.1%
15A	47	3.0%
23B	47	3.0%
24	45	2.9%
10A"	45	2.9%
23A	41	2.6%
6C	40	2.5%
33F"	36	2.3%
11A"	26	1.7%
7F**	23	1.5%
20"	19	1.2%
35B	18	1.1%
14*	18	1.1%
31	17	1.1%
24F	17	1.1%
9L	17	1.1%
17F"	17	1.1%
34	15	1.0%
16	14	0.9%
38	13	0.8%
7B	12	0.8%
15B"	12	0.8%
35	9	0.6%
1**	9	0.6%
16F	8	0.5%
24A	8	0.5%
21	6	0.4%
4*	6	0.4%
10B	4	0.3%
15C	4	0.3%
18A	4	0.3%
35F	4	0.3%

13	3	0.2%
29	3	0.2%
24B	3	0.2%
23F*	3	0.2%
27	2	0.1%
18F	2	0.1%
33A	2	0.1%
5**	2	0.1%
6	1	0.1%
32	1	0.1%
10F	1	0.1%
12B	1	0.1%
15F	1	0.1%
16A	1	0.1%
22A	1	0.1%
7C	1	0.1%
6A***	1	0.1%
18C*	1	0.1%
6B*	1	0.1%
9V*	1	0.1%
non typable	7	0.4%
TOTAL	1571	100%

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

bacteremia and pleuritis (n=1489)			meningitis (n=68)			otitis media (n=39)		
serotype	number	percentage	serotype	number	percentage	serotype	number	percentage
8	252	16,9%	3	9	14,5%	19A	10	25,6%
3	182	12,2%	12F	9	14,5%	3	7	17,9%
19A	161	10,8%	8	8	12,9%	11A	6	15,4%
12F	127	8,5%	23B	4	6,5%	19F	3	7,7%
			6C	4	6,5%	10A	2	5,1%
						23B	2	5,1%
						33F	2	5,1%

Table 7: Evolution of pneumococcal antibiotic non-susceptibility (1987-2018) 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
	N=433	N=382	N=520	N=540	N=536	N=552	N=641	N=751	N=992	N=1289
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
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)
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)
Ofloxacin/Levofloxacin	-	-	-	-	-	-	-	-	4(0.4)	0
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)

* strains with MIC penicilline > 0.06 mg/L

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
	N=1241	N=1205	N=1216	N=1218	N=1427	N=1542	N=1917	N=1744	N= 1737	N=1609	N=1726
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
124(10)	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)	
288(23.2)	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)	
3(0.2)	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)	
355(28.6)	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)	

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
	N=1870	N=2044	N=1992	N=1998	N=1841	N=1729	N=1269	N=1445	N=1384	N=1544	N=1614
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
172 (9.2)	152 (7.4)	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)	
449 (24.0)	502 (24.5)	512(25.7)	552 (27.6)	533 (28.9)	412 (23.8)	230 (18.1)	241 (16.7)	190 (13.7)	221 (14.3)	169 (16.7)	
5 (0.3)	4 (0.2)	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)	
477 (25.5)	496 (24.3)	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%)	

Table 8: Antibiotic non-susceptibility for penicillin, erythromycin and tetracyclin per serotype/serogroup for all IPD isolates sent to the National Reference Centre in 2018. *For penicillin non-susceptibility is defined by MIC penicillin > 0,06 mg/L.

Serotype/ serogroup	Total number of strains	penicillin*		erythromycin		tetracycline	
		number of non- susceptible strains	% non- susceptible	number of non- susceptible strains	% non- susceptible	number of non- susceptible strains	% non- susceptible
8	264	1	0%	1	0%	5	2%
3	196	1	1%	7	4%	9	5%
19A	166	29	17%	43	26%	45	27%
12F	137	0	0%	6	4%	39	28%
9N	62	1	2%	0	0%	3	5%
22F	58	0	0%	2	3%	1	2%
19F	48	9	19%	38	79%	13	27%
15A	47	7	15%	15	32%	13	28%
23B	47	21	45%	2	4%	2	4%
24	45	30	67%	30	67%	25	56%
10A	45	1	2%	1	2%	3	7%
23A	41	2	5%	6	15%	5	12%
6C	40	2	5%	24	60%	24	60%
33F	36	0	0%	16	44%	11	31%
11A	26	10	38%	2	8%	3	12%
7F	23	0	0%	1	4%	2	9%
20	19	0	0%	0	0%	0	0%
14	18	12	67%	8	44%	3	17%
35B	18	4	22%	7	39%	5	28%
31	17	0	0%	4	24%	4	24%
17F	17	0	0%	0	0%	1	6%
24F	17	12	71%	12	71%	11	65%
9L	17	1	6%	1	6%	0	0%
34	15	1	7%	1	7%	0	0%
16	14	0	0%	0	0%	0	0%
38	13	0	0%	0	0%	0	0%
15B	12	1	8%	4	33%	4	33%
7B	12	0	0%	0	0%	1	8%
1	9	0	0%	0	0%	1	11%
35	9	0	0%	1	11%	0	0%
16F	8	0	0%	0	0%	0	0%
24A	8	6	75%	6	75%	6	75%
4	6	0	0%	0	0%	1	17%
21	6	0	0%	0	0%	0	0%
10B	4	0	0%	0	0%	0	0%

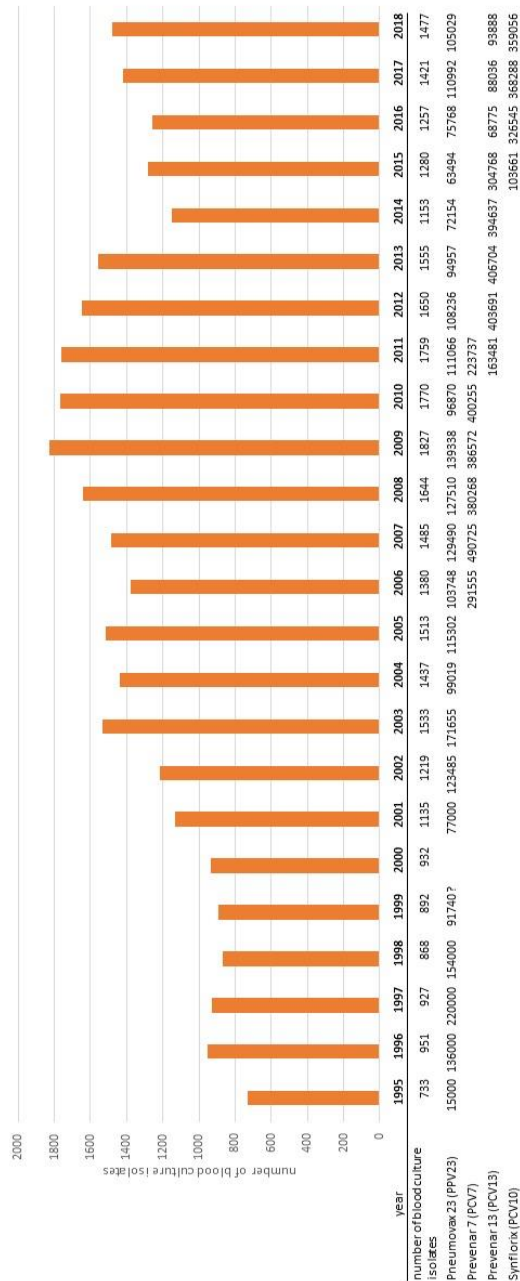
15C	4	0	0%	0	0%	0	0%
18A	4	0	0%	0	0%	1	25%
35F	4	0	0%	0	0%	0	0%
13	3	0	0%	0	0%	0	0%
29	3	2	67%	1	33%	1	33%
23F	3	2	67%	3	100%	3	100%
24B	3	1	33%	1	33%	1	33%
5	2	0	0%	0	0%	0	0%
27	2	0	0%	0	0%	0	0%
18F	2	0	0%	0	0%	0	0%
33A	2	0	0%	2	100%	1	50%
6	1	0	0%	0	0%	0	0%
32	1	0	0%	0	0%	0	0%
10F	1	0	0%	0	0%	0	0%
12B	1	0	0%	0	0%	1	100%
15F	1	0	0%	0	0%	0	0%
16A	1	1	100%	1	100%	1	0%
18C	1	0	0%	0	0%	0	0%
22A	1	0	0%	0	0%	0	0%
6A	1	1	100%	1	100%	0	100%
6B	1	0	0%	1	100%	1	0%
7C	1	0	0%	0	0%	0	0%
9V	1	0	0%	0	0%	0	100%
non typable	7	3	43%	4	57%	2	29%
Total	1571	161	10%	252	16%	252	16%

Table 9: Evolution of pneumococcal antibiotic resistance per infection localisation (1999-2018) based on susceptibility testing of all pneumococcal strains received at the National Reference Centre (IPD strains plus strains from patients with otitis media). *For penicillin non-susceptibility is defined by MIC penicillin > 0,06 mg/L.

		% strains non-susceptible		
		penicilline G*	tetracycline	erythromycin
Blood + pleura	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
	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	
cerobrospinal fluid	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
	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	

% strains non-susceptible				
		penicilline G*	tetracycline	erythromycin
	1999	29.3	40	50.7
	2000	28.6	40.6	49.5
	2001	27.4	37.4	49.3
	2002	26.5	37.4	50.2
	2003	21.6	39.6	52.2
	2004	24.6	34.7	52.8
	2005	25.7	29.4	35.8
	2006	18.8	36.6	38.6
	2007	18.7	40.2	38.4
middle ear fluid	2008	15.2	34.8	40.2
	2009	21.7	42.2	45.8
	2010	26.2	36.9	36.9
	2011	27.5	38.4	41.8
	2012	35.4	43.7	43.7
	2013	29.5	34.1	40
	2014	26.2	16.2	27
	2015	19.2	13.4	28.8
	2017	34.4	20.6	34.4
	2017	35.0	15.0	35.0
	2018	35.9	38.5	38.5

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 1995-2018.



Acknowledgements

Technicians performing the capsular typing and susceptibility testing: K. Verheyden, K. Willems, A. Ghyselinck, K. Standaert and M. Vanhelfmont

Secretary of the National Reference Centre for invasive *S. pneumoniae*: M. Charlier and S. Wuyts
 Prof. em. Jan Verhaegen for helping with the writing and reviewing of this report and Prof. Katrien Lagrou for reviewing the report.