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Report National Reference Centre invasive *Streptococcus pneumoniae* 2024

This is the report of the National Reference Centre (NRC) for invasive *Streptococcus pneumoniae* UZ Leuven with a focus on invasive pneumococcal disease (IPD) isolates from the year 2024.

1. Characteristics of surveillance in 2024

Data of the NRC are based on a passive laboratory-based surveillance. We performed capsular typing (Quellung reaction, antisera SSI Diagnostica) to determine the pneumococcal serotype and assessed the antimicrobial susceptibility of all invasive *S. pneumoniae* strains sent to the NRC. This surveillance is not focused on non-invasive *S. pneumoniae* isolates (i.e. isolated from BAL, middle ear, sputum, ...).

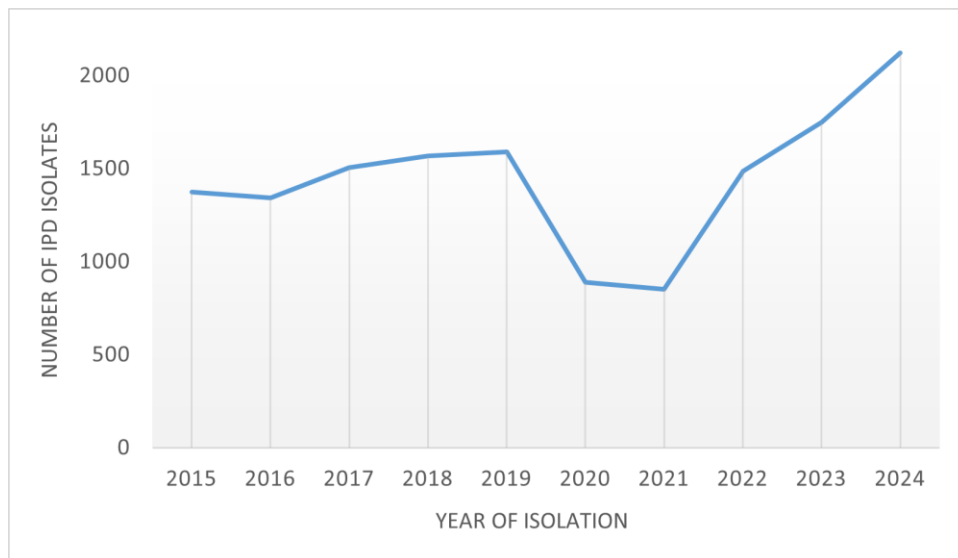


Figure 1: Evolution of the number of IPD isolates received at the NRC from 2015 to 2024.

For both years 2020 and 2021, the pneumococcal epidemiology was disturbed (Figure 1), followed by a re-increase of invasive pneumococcal isolates in 2022. Throughout 2023 (Figure 2), a high number of strains was analysed (N=1750), being the highest number of isolates that the NRC was confronted with since 2012. However, in the year 2024 all records were broken, with a total number of 2120 IPD isolates received. For all months in 2024 ([report *S. pneumoniae* 2024 Q1-Q2](#)), except for November, IPD case counts increased those of 2023 and of the mean of pre-COVID (2015-2019). An exceptional high number of isolates was observed for December, totalling 345 cases, being the highest monthly case count since the start of the IPD surveillance in 1996 ([communication January 2025](#)).

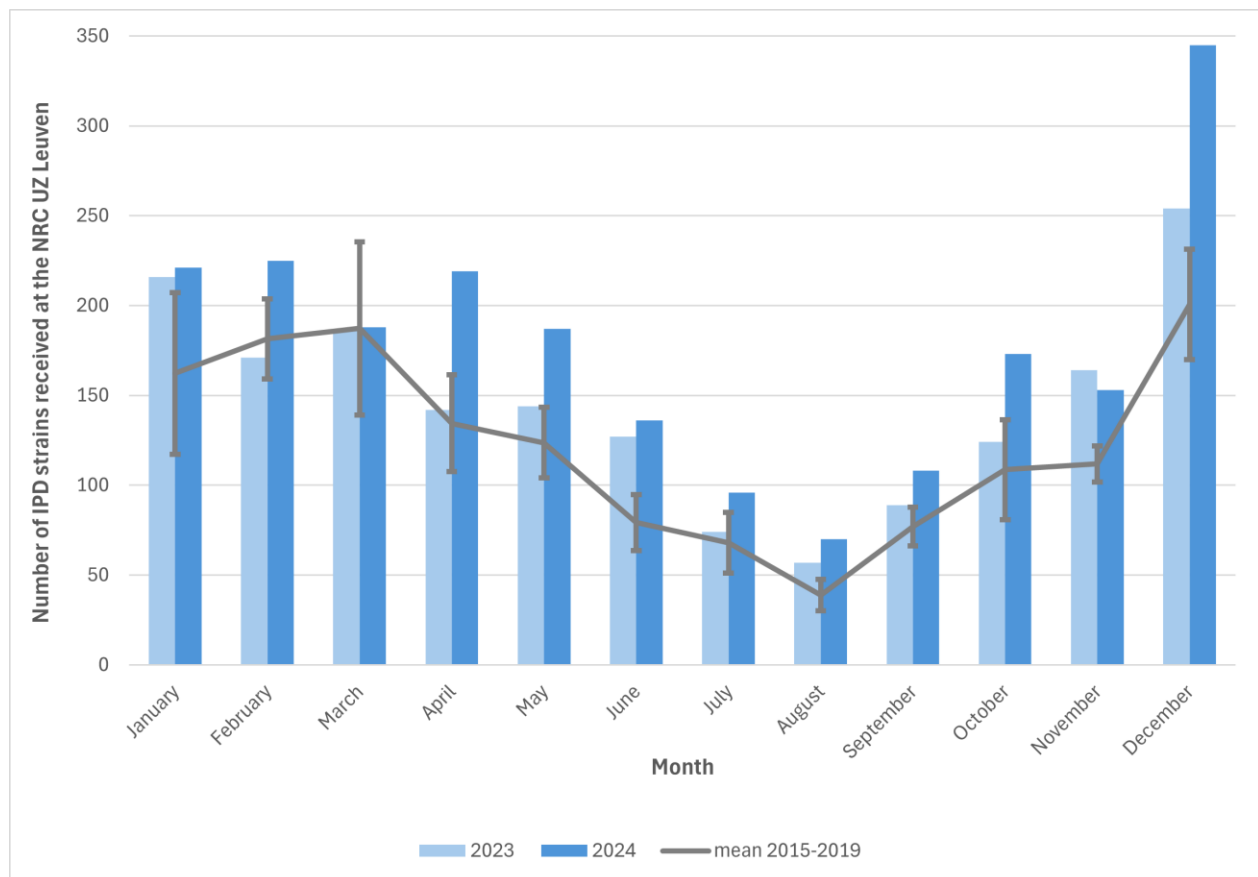


Figure 2: The number of IPD isolates received at the NRC per month for the years 2023 and 2024, in comparison to the mean number of IPD isolates received between pre-COVID years 2015 to 2019.

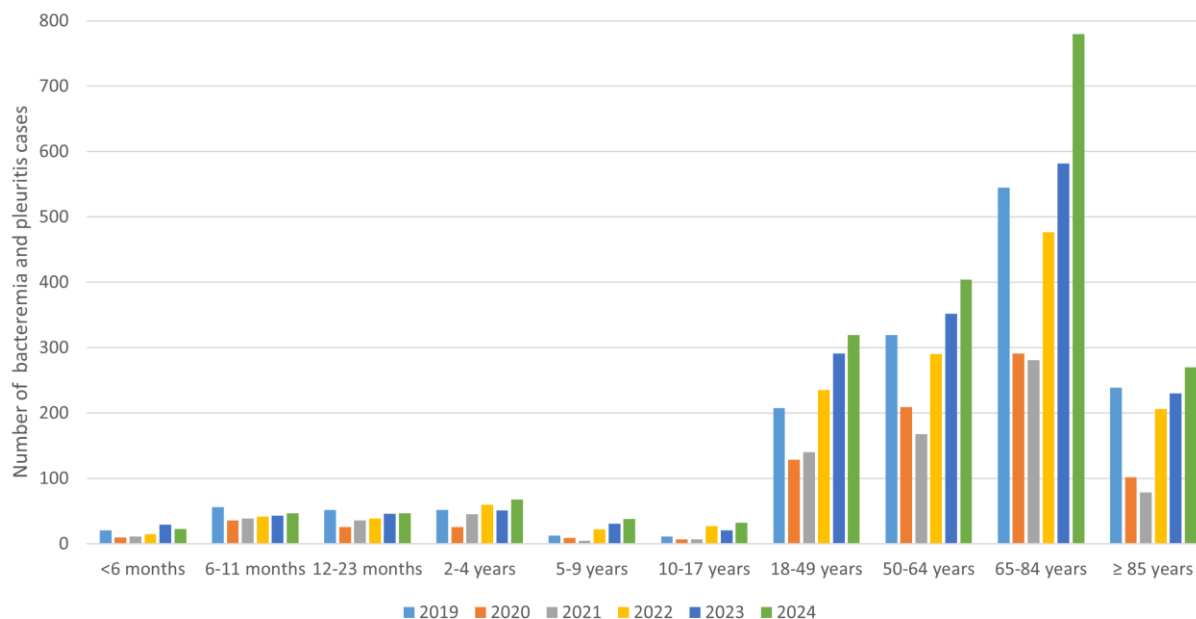
The decreasing trend for the years 2020 and 2021,^{1,2} followed by the years 2022 and 2023 with again an increasing number of infections, in line with pre-COVID years; is unexpected. It is assumed that the surveillance itself remained stable for all years, despite disturbance by the COVID-19 epidemic. In 2024, the number of different participating laboratories (n=87, considering all strains received at the NRC, not specifically focused on IPD), as well as the number of laboratories sending more than 5 strains (n=73) to our NRC, normalized again compared to the pre-COVID year 2019 (Table 1).

Table 1: Characteristics of the surveillance of the Belgian National Reference Centre invasive *S. pneumoniae* during the period of 2019-2024. (IPD: invasive pneumococcal disease; *considering mergers of laboratories)

	2019	2020	2021	2022	2023	2024
number of unique IPD isolates sent to the NRC	1591	888	852	1487	1750	2120
number of laboratories* involved in surveillance						
all	92	93	85	88	91	87
sending more than 5 isolates per year	70	55	57	71	74	73
located in Flanders	54	55	50	52	49	46
located in Wallonia	28	28	26	27	33	32
located in Brussels	10	10	9	9	9	9
regional distribution of all isolates based on residence of patient (percentage)						
Flanders	66,8%	64,3%	58,2%	57,9%	56,3%	57,2%
Wallonia	23,3%	25,4%	24,8%	26,6%	29,7%	30,7%
Brussels	9,3%	8,8%	13,9%	11,2%	11,2%	9,6%
other/unknown	0,5%	1,5%	3,1%	4,3%	2,9%	2,5%

A total of 2221 streptococcal strains, with 2120 unique IPD strains, were received in 2024. A majority of the strains were isolated from blood cultures (94.6%) and cerebrospinal fluid (3.7%). More IPD strains were identified from males (53.4%) compared to females (46.4%).

a



b

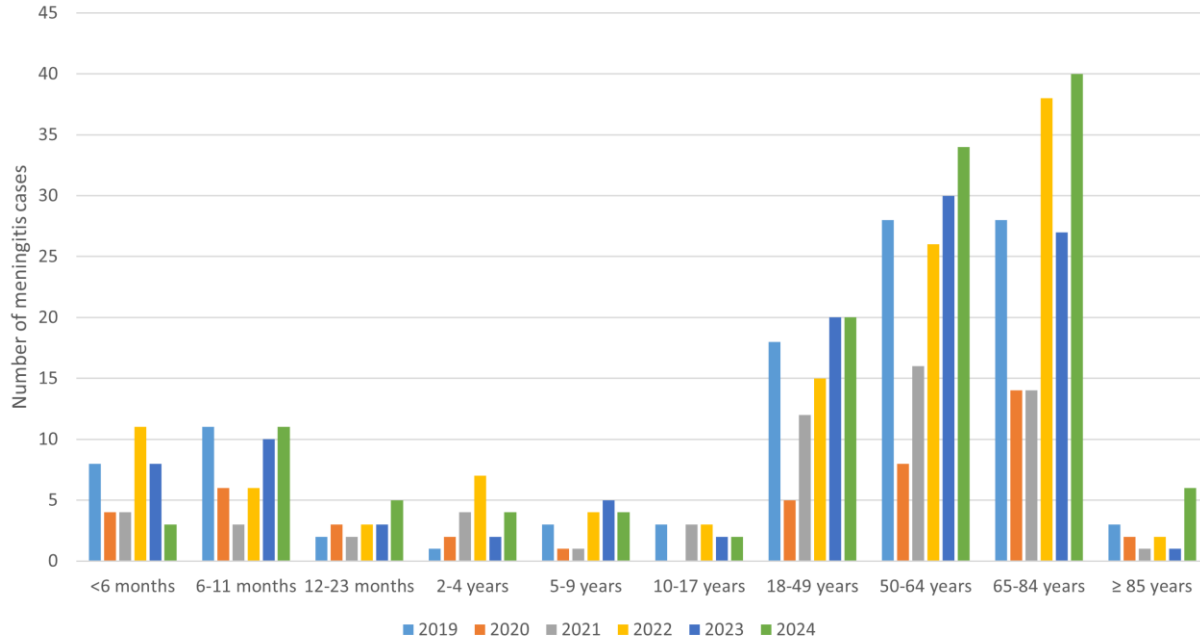


Figure 3: Evolution of the number of (a) bacteraemia/pleuritis cases based on origin of isolation and (b) meningitis cases based on clinical diagnosis, based on *S. pneumoniae* isolates sent to the NRC per age group, for the years 2019-2024. Bacteraemia/pleuritis: isolation of *S. pneumoniae* from blood culture and/or pleural fluid. Meningitis: clinical diagnosis; which are both cases with isolation of *S. pneumoniae* from cerebrospinal fluid and meningitis cases without a strain received from CSV but with indication of meningitis as clinical presentation.

Figure 3 indicates the age distribution of patients from whom pneumococci were isolated from one of the three major infection sites (blood, pleural fluid and cerebrospinal fluid) and/or clinically diagnosed with meningitis. For bacteraemia and pleuritis cases, compared to 2023, the number of isolates has increased for nearly all age groups excepted for those <6 months of age. The large increase of overall IPD in 2024 is mainly due to the high number of bacteraemia/pleuritis cases in the age group 65-84 years old.

A total number of 78 meningitis cases, based on isolation of *S. pneumoniae* from cerebrospinal fluid, was observed for the year 2024, which is 20 cases more than in 2023. When considering meningitis based on clinical diagnosis, and therefore not limiting the definition to isolation from cerebrospinal fluid, the number of cases is substantially higher (+40%), with 130 cases indicated as meningitis (Figure 3b). In comparison with 2023 (n=106), 24 additional meningitis cases were observed. The higher number of meningitis cases compared to 2023 was observed for the following age groups: 6-11 months, 12-23 months, 2-4 years, 50-64 years, 65-84 years and >85 years, with increases of >30% for 12-23 months, 2-4 years, 65-84 years and >85 years. Results must be interpreted with caution since the absolute number of meningitis cases is low in certain age groups and year-to-year fluctuations are observed. Nevertheless

the increasing absolute number of meningitis cases (while the proportion remained stable: 6.1% for both years 2023 and 2024) is worrisome and will be followed further by the NRC.

2. Serotype distribution of invasive pneumococcal isolates

2.1. All ages

Table 2 describes in descending order of frequency the serotypes of IPD isolates detected in 2024. The serotype distribution is determined per age group. Overall, serotype 12F is the most prevalent serotype responsible for 14.6% of the IPD isolates in 2024. Serotypes 8 (11.5%), 3 (9.4%), 4 (7.7%) and 19A (6.8%) complete the top 5 of most frequently detected serotypes. Focusing solely on the 130 meningitis cases clinically diagnosed among all age groups, the top 5 of most frequently detected serotypes is somewhat different: serotype 12F (16.2%), serotypes 3 and 23B (each 6.9%), serotype 4 (6.2%) and serotypes 24F and 33F (each 5.4%).

Table 2: Distribution of serotypes of IPD isolates from 2024 (n=2120) per age group. (colour code: orange/red: highest proportion, yellow: intermediate proportion, dark green: lowest proportion; PCV7: PCV7 serotypes (4, 6B, 9V, 14, 18C, 19F, 23F); PCV10: PCV10 non-PCV7 serotype: 1, 5, 7F; PCV13: PCV13 non-PCV10 serotype: 3, 6A, 19A; PCV15: PCV15 non-PCV13 serotypes: 22F, 33F; PCV20: PCV20 non-PCV15 serotypes: 8, 10A, 11A, 12F, 15B; PPV23: PPV23 only serotypes: 2,9N, 17F, 20, NVT: non-PCV20 serotype)

serotype		<18 years (n=278)	18-49 years (n=335)	50-64 years (n=426)	65-84 years (n=805)	>85 years (n=273)	all ages (n=2120)
12F	PCV20	19,8%	16,1%	16,4%	12,8%	10,3%	14,6%
8	PCV20	6,1%	13,4%	14,3%	12,5%	7,3%	11,5%
3	PCV13	5,4%	9,9%	8,0%	11,1%	9,9%	9,4%
4	PCV7	0,4%	21,2%	11,0%	4,7%	1,8%	7,7%
19A	PCV13	7,6%	6,3%	6,6%	6,3%	8,8%	6,8%
14	PCV7	6,8%	6,3%	3,8%	6,1%	7,3%	5,9%
9N	PPV23	2,5%	3,0%	6,8%	5,2%	6,2%	5,0%
22F	PCV15	2,9%	2,7%	3,5%	5,2%	4,4%	4,1%
24F	NVT	10,8%	1,8%	2,1%	3,2%	4,8%	4,0%
33F	PCV15	7,2%	0,6%	3,1%	3,1%	4,4%	3,3%
15A	NVT	2,2%	1,5%	1,6%	3,7%	2,2%	2,5%
6C	NVT	0,4%	2,7%	1,9%	2,5%	5,9%	2,5%
23B	NVT	3,2%	1,2%	2,1%	3,0%	2,6%	2,5%
11A	PCV20	4,0%	0,6%	1,9%	2,5%	2,6%	2,3%
16F	NVT	1,1%	1,5%	1,6%	3,0%	2,2%	2,1%
10A	PCV20	2,9%	1,8%	1,9%	2,0%	2,2%	2,1%
23A	NVT	1,8%	0,6%	1,2%	1,9%	3,3%	1,7%
31	NVT	0,4%	0,9%	1,2%	1,4%	1,8%	1,2%
7B	NVT	2,5%	0,3%	0,9%	1,1%	1,1%	1,1%
15B	PCV20	0,4%	0,6%	1,4%	1,4%	1,5%	1,1%

7C	NVT	2,5%	0,3%	0,9%	1,1%	0,7%	1,1%
19F	PCV7	1,4%	0,6%	1,2%	1,2%	0,7%	1,1%
35B	NVT	0,7%	0,3%	0,7%	1,1%	1,5%	0,9%
35F	NVT	0,4%	1,5%	0,0%	0,9%	1,8%	0,8%
20	PPV23	0,4%	0,3%	1,2%	0,4%	0,7%	0,6%
other serotypes (< 0.5% all ages)		6,5%	4,2%	4,7%	2,6%	4,0%	4,1%

Following an initial increase in 2023, serotype 12F gained even more importance in 2024, increasing from an overall proportion of 7.3% (ranked 6th) to 14.6% among all age groups. The increase of 12F infections is even more strongly pronounced when looking at absolute numbers, showing an increase from 134 cases in 2023 to 310 in 2024. Serotypes 3, 4, 8 and 19A slightly decreased in serotype proportion compared to 2023, however, in absolute numbers serotypes 4 and 19A remained stable, while the absolute number of serotype 3 and 8 increased compared to 2023 (+34.2% and 39.3% respectively).

Other increases for the overall serotype distribution in 2024 compared to 2023 are observed for serotypes 9N (+1.9%), 14 (+3.7%) and 24F (+1.1%). While increases are relatively modest with respect to overall proportions, the absolute number of IPD cases almost or more than doubled for serotypes 14 and 9N, respectively from 28 to 125 cases, and from 54 to 105 cases. For serotype 24F, the number of IPD cases increased from 51 in 2023 to 84 in 2024. While in 2023 the largest increase in overall serotype distribution was observed for serotype 22F, the latter decreased again in 2024 (8.2% to 4.1%). Notably, all serotypes (except for serotype 24F) that show the largest changes in overall serotype distribution or absolute number of IPD infections between 2023 and 2024, are vaccine serotypes; with serotypes 4 and 14 included in PCV7, serotypes 3 and 19A in PCV13, serotypes 8 and 12F in PCV20, and serotype 9N in PPV23. While serotype 4 showed a continued increase in absolute number of IPD infections since 2019³, a plateau seems to be reached in 2024. Due to the exponential increase of serotype 14 IPD infections, a representative selection of isolates is currently being investigated using whole-genome sequencing.

Differences in serotype distribution are observed among the different age groups. The largest difference in serotype proportion between children (<18 years old) and older adults (>85 years old) was noted for serotype 12F (19.8% versus 10.3%). When comparing children (<18 years old) with adults (50-64 years), large differences were observed in the distribution for serotypes 8 (6.1% versus 14.3%), 14 (6.8% vs 3.8%) and 9N (2.5% versus 6.8%). When comparing children and older adults (65-84 years), serotype 3 is notable (5.4% versus 11.1%). However, the difference in serotype distribution is most pronounced for serotype 4 between children (<18 years) and younger adults (18-49 years) (0.4% versus 21.2%), while the opposite is true for serotypes 24F and 33F (10.8% versus 1.8%, and 7.2% versus 0.6%, respectively).

The two most recent pneumococcal conjugate vaccines (PCVs) that were approved for use in children and adults, are the 15-valent (PCV15) and the 20-valent pneumococcal conjugate vaccine (PCV20). The most recent advices of the Superior Health council regarding pneumococcal immunisation for adults and children can be found online (<https://www.hgr-css.be/en/reports>).

In Figure 4, we analysed the theoretical serotype coverage of the four currently available vaccines (PCV13, PCV15, PCV20 and the 23-valent polysaccharide vaccine (PPV23)) based on the serotype

distribution of the invasive pneumococcal strains per age group in 2024. The proportion of PCV15 non-PCV13 serotype and PCV20 non-PCV13 serotype IPD ranges respectively from 3.3% to 10.1% and 32.6% to 43.2% depending on the age group. It has to be taken into account that serotype 3 is a serotype included in PCV13, PCV15 and PCV20, despite their low or unclear effectiveness to protect against this important serotype. Despite changes in serotype distribution, the theoretical serotype coverage of the different vaccines remained mainly comparable to 2023.

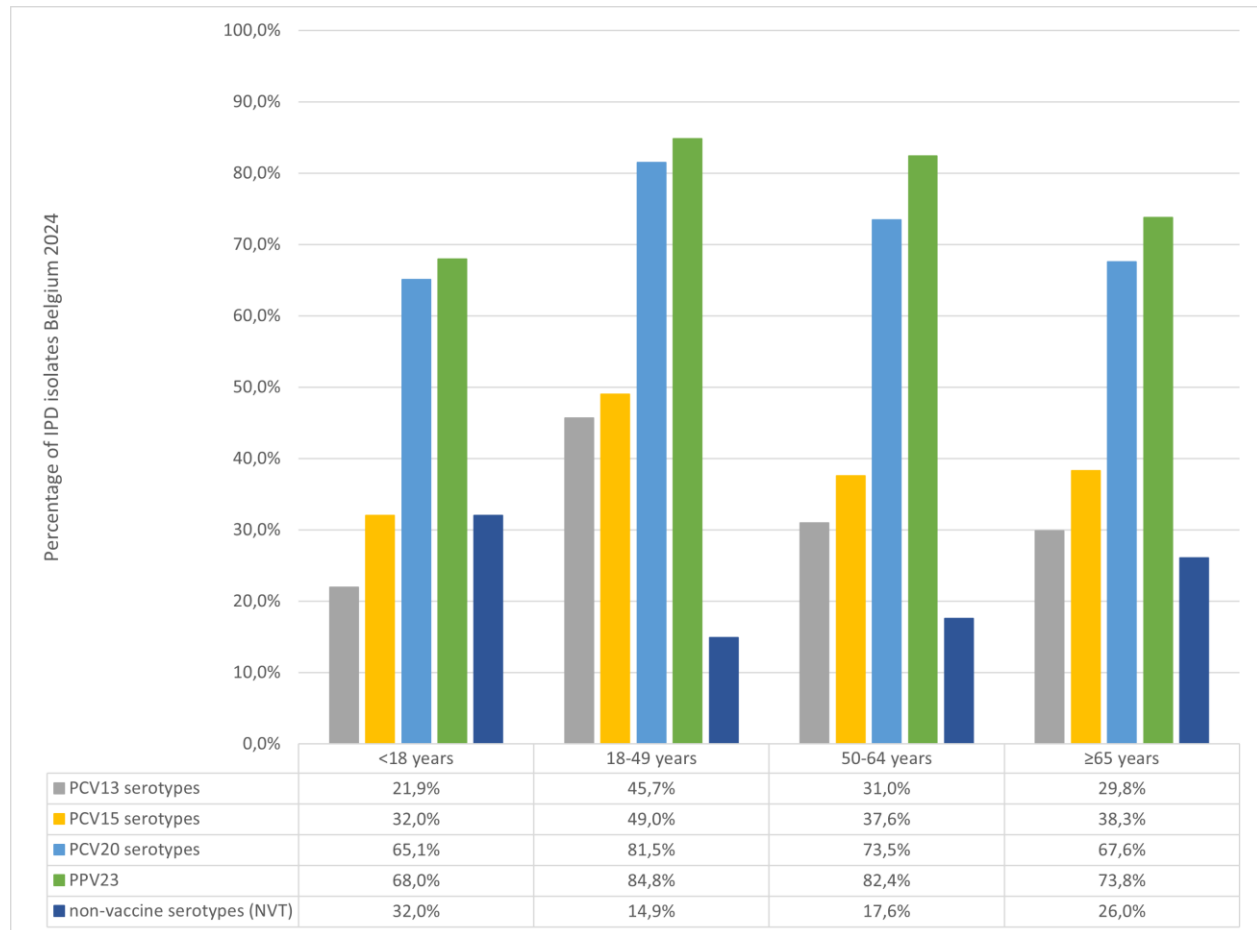


Figure 4: Serotype coverage of the current authorized pneumococcal vaccines per age group based on the invasive pneumococcal disease isolates received at the National Reference Centre in 2024. NVT: non-PPV23 and non-PCV20 serotypes (*Figure updated in this version of the report – April 2025*).

2.2. Children < 2 years old

In 2024, 134 invasive pneumococcal isolates from children <2 years old were received at the NRC. This number is in line with 2023, when 128 IPD isolates were reported. In children <6 months (n=25), children aged 6-11 months (n=58) and children 12-23 months (n=51) old the number of cases were also in line with data from 2023.

Table 3 indicates the serotype distribution of invasive isolates in children during the first two years of life by capsular type in 2024. The predominant serotypes in 2024 (with a proportion >5%) are serotypes 24F (16.4%), 12F (13.4%), 33F (12.7%), 3 (6.0%), 19A (6.0%), and 7B (5.2%). Compared to 2023, when serotypes 10A and 15B were characterised with a proportion >5%, serotype 10A decreased to 4.5% in 2024 and serotype 15B was no longer detected. When focusing on the 19 meningitis cases clinically diagnosed in these young children, serotype 33F was detected in five cases, and serotypes 12F and 24F both each in three cases, while for the other 8 cases unique serotypes were found (serotypes 7B, 10A, 15A, 16F, 18C, 19A, 23B, and 35F).

Table 3: Serotypes causing IPD in children <2 years old in 2024 categorized based on their inclusion in pneumococcal conjugate vaccines *non-PCV20 serotypes only detected in one strain (<1%)

serotype	number	%
PCV7	7	5,2%
14	2	1,5%
18C	1	0,7%
19F	4	3,0%
PCV13 non-PCV10	16	11,9%
3	8	6,0%
19A	8	6,0%
PCV15 non-PCV13	22	16,4%
22F	5	3,7%
33F	17	12,7%
PCV20 non-PCV15	32	23,9%
8	3	2,2%
10A	6	4,5%
11A	5	3,7%
12F	18	13,4%
non-PCV20 serotypes	57	42,5%
24F	22	16,4%
7B	7	5,2%
24B	5	3,7%
7C	5	3,7%
15A	3	2,2%
23B	3	2,2%
33A	2	1,5%
16F	2	1,5%
9N	2	1,5%
other*	6	4,5%
TOTAL	134	100,0%

The proportion of serotype 19A infections continued to decrease in 2024 (-4.2% versus 2023 and -8.0% versus 2022), following re-introduction of PCV13 in 2019. Increasing proportions were observed for serotypes 24F (+5.5%), 12F (+4.0%) and 3 (+3.7%) compared to 2023, while a decreasing trend was observed for serotype 10A (-6.4%). The largest increase in proportion of vaccine serotypes was seen for the group of PCV7, moving from only one case (0.8%) in 2023 to 7 cases in 2024 (5.2%); the latter mainly due to four 19F IPD infections in children (2 cases in children <6 months old and 2 cases in children 6-11 months old). A decrease in the proportion of PCV20 non-PCV15 serotypes from 28.9% in 2023 to 23.9% in 2024 was observed (respectively from 27.8% in 2023 to 20.0% for <6 months old, from 25.5% to 19.0% for 6 to 11 months old, and from 31.9% to 31.4% for 12-23 months old), while the serotype coverage of other PCVs remained mainly stable. In 2024, still 17.1% of cases were caused by serotypes included in PCV13 of which we know one patient was completely vaccinated with PCV13 (2+1; serotype 19A).

3. Antimicrobial susceptibility of pneumococcal isolates

Table 4 illustrates the evolution of resistance of pneumococcal isolates 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 as screening method. In case of a positive oxacillin screen (oxacillin diameter <20 mm), MICs are determined for penicillin, amoxicillin and cefotaxime. Until July 2020, MICs were determined by Etest (BioMérieux, France). From the first of August 2020 on, MICs were determined by broth microdilution (Sensititre, ThermoScientific, USA). This change in method was situated in the context of a warning of EUCAST against the use of gradient tests to determine MICs of penicillin (November 2019). In their study, gradient tests (Etest and MTS) frequently underestimated penicillin MIC values by one or more doubling dilutions. This observation was also confirmed by a recent multicentre study coordinated by the NRC and the National Antibiogram Committee (NAC)⁴. This underestimation is detrimental in the important area close to the R breakpoint (R> 0.06 mg/L) used in our report and the R clinical breakpoint for non-meningitis (MIC > 2 mg/L). In accordance with the new definition of 'I' of EUCAST, the strains categorized as I were counted together with S categorized strains.

Three hundred eighteen (15.0%) of the 2120 IPD strains showed a reduced susceptibility to penicillin (MIC >0.06 mg/L= EUCAST epidemiological cut-off and meningitis R breakpoint), which is somewhat higher than last year. Fifty-four of these 318 strains had a penicillin MIC above 2 mg/L (non-meningitis R breakpoint). For cefotaxime, the resistance rates are stable compared to last year. Seventy-five strains (3.5%) had a cefotaxime MIC >0.5 mg/L (EUCAST meningitis R breakpoint). Only four strains had a MIC above 2 mg/L and were categorized as resistant following the EUCAST non-meningitis breakpoint. Among the isolates with reduced susceptibility to penicillin in 2024, six serotypes accounted each for 10% or more of the isolates, more specifically serotypes 24F, 23B, 11A, 6C, 19A and 14.

When only focussing on strains isolated from patients with meningitis (n=130): 23 strains were penicillin resistant (17.7%), 3 strains (2.3%) were amoxicillin resistant and 2 strains (1.5%) were cefotaxime resistant according to EUCAST clinical breakpoints for meningitis. Both cefotaxime resistant isolates had a cefotaxime MIC of 1 mg/L which is close to the breakpoint (R>0.5 mg/L), with serotypes 11A and 15A.

The erythromycin (16.7%) resistance rate in 2024 somewhat increased compared to the rate observed in 2023, while for tetracycline (18.4%) the resistance rate remains in line with 2023. Levofloxacin resistance remains rare, with no isolates interpreted as resistant in 2024.

Table 4: Antibiotic resistance rates of all unique invasive pneumococcal strains received at the NRC from 2018-2024. *change of method mid 2020 (cells coloured in grey for the years 2018-2020).

antibiotic	2018 n=1571 (%)	2019 n=1592 (%)	2020* n=884 (%)	2021 n=863 (%)	2022 n=1487 (%)	2023 n=1747 (%)	2024 N=2120 (%)
penicillin R							
penicilline MIC > 0.06 mg/L	10.2%	9.9%	15.0%	18.4%	14.3%	13.3%	15.0%
penicilline MIC > 2 mg/L	0.0%	0.0%	1.2%	3.6%	2.0%	1.8%	2.5%
cefotaxime R							
cefotaxime MIC > 0.5 mg/L	0.2%	0.6%	2.1%	4.9%	3.5%	3.4%	3.5%
cefotaxime MIC > 2 mg/L	0.0%	0.1%	0.2%	0.7%	0.2%	0.1%	0.2%
tetracycline R	14.0%	14.4%	18.8%	15.1%	14.1%	18.1%	18.4%
levofloxacin R	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.0%
erythromycin R	15.3%	15.8%	19.8%	16.5%	14.7%	14.9%	16.7%

4. Pneumococcal vaccines

During the last 10 years, different changes in the childhood immunization programmes were made. In 2015 (in the Flemish region) and in 2016 (Walloon region) PCV13 was replaced by PCV10. In summer of 2019, PCV10 was again replaced by PCV13. The number of vaccines sold for immunization of children remained overall stable (see Table 5).

Table 5: Evolution of the number of blood culture isolates received at the NRC and the number of the different vaccines sold in Belgium for 2019-2024. (source: personal communication with Pfizer Belgium and MSD Belgium). (*ex-factory doses PCV13 in 2023: paediatric: 345613; adult: 6673; in 2024: paediatric: 332761; adult: 3323, not taking into account parallel import)

Year	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Number of blood culture isolates	1280	1257	1421	1477	1503	837	817	1401	1692	2010
Pneumovax (PPV23)	63494	75768	110992	105029	122604	152950	185991	76445	55728	52242
Synflorix (PCV10)	103661	326545	368288	359056	209962					
Prevenar 13 (PCV13)	304768	68775	88036	93888	126420	518016	406278	364844	352286*	336084*
Vaxneuvance (PCV15)								873	514	183
Apexxnar (PCV20)								33111	89895	116723

For adult pneumococcal immunisation in Belgium in 2024, four vaccines could be used in theory: PPV23, PCV13, PCV15 and PCV20, with the latter currently recommended as first choice. The number of PPV23 vaccine doses sold in 2024 slightly further decreased by about 6% compared to 2023. Probably thanks to the reimbursement of PCV20, an increase in PCV20 vaccines sold in Belgium (+30% compared to 2023) was observed. Despite this increase, still a low overall vaccination rate in adult risk groups is estimated, which is in contrast to the high vaccination rate in the youngest children (94% for the third dose).

5. References

- [1] Brueggemann AB, Jansen van Rensburg MJ, Shaw D, *et al.* Changes in the incidence of invasive disease due to *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis* during the COVID-19 pandemic in 26 countries and territories in the Invasive Respiratory Infection Surveillance Initiative: a prospective analysis of surveillance data. *Lancet Digit Health* 2021;3(6):e360-e370.
- [2] Shaw D, Abad R, Amin-Chowdhury Z, *et al.* Sustained reductions in life-threatening invasive bacterial diseases during the first two years of the COVID-19 pandemic: analyses of prospective surveillance data from 30 countries participating in the IRIS consortium. *medRxiv preprint* 2022.
- [3] Cuypers L, Menten B, Sanchez GJ, *et al.* Rapid increase of vaccine serotype 4 (GPSC162) invasive pneumococcal disease in young adults since 2020 in Belgium. Abstract accepted as poster presentation for ISSPD 2024, South-Africa, March 2024.
- [4] Martens S, Cuypers L, Bélik F, *et al.* Multicenter comparison of Etest, Vitek2 and BD Phoenix to broth microdilution for beta-lactam susceptibility testing of *Streptococcus pneumoniae*. *Eur J Clin Microbiol Infect Dis*. 2024;43(7):1375-1381.

6. Acknowledgements

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