NETHERLANDS REFERENCE LABORATORY FOR BACTERIAL MENINGITIS

BACTERIAL MENINGITIS IN THE NETHERLANDS

ANNUAL REPORT 2024

Amsterdam UMC

Reference Laboratory Bacterial Meningitis
AMC RIVM
Amsterdam
The Netherlands

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Netherlands Reference Laboratory for Bacterial Meningitis (AmsterdamUMC/RIVM)
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CONTENTS

1 INTRODUCTION

This is the **53st** Annual Report of the Netherlands Reference Laboratory for Bacterial Meningitis (NRLBM) of the Amsterdam UMC and the National Institute of Public Health and the Environment (RIVM). The NRLBM is located within the Department of Medical Microbiology and Infection Prevention of the Amsterdam UMC in Amsterdam, The Netherlands. The NRLBM collaborates with all Dutch clinical microbiology laboratories that submit bacterial isolates and/or biological samples (e.g. cerebrospinal fluid, CSF) from patients with meningitis as well as other invasive diseases and we are most grateful to our colleagues for their collaboration and dedication.

The NRLBM started collecting isolates of *Neisseria meningitidis* in 1959 and of other meningitis-causing bacterial species in 1975. In the archives of the NRLBM isolates of approximately 104,000 patients are now available for studies on the epidemiology of invasive bacterial infections, particularly bacterial meningitis, and on the pathogenicity and antibiotic susceptibility of isolates.

The objectives of the NRLBM are:
- to perform surveillance of invasive bacterial infections with a longstanding focus on bacterial meningitis;
- to describe the (molecular) epidemiology of invasive bacterial infections;
- to provide insights on vaccine coverage and leads for the development of potential vaccine components;
- to provide data about antibiotic susceptibility of isolates.

The information is presented in tables and figures and shortly discussed in the text.

We welcome your opinion and suggestions on this report.

Amsterdam, August, 2025

I.G.A. de Beer - Schuurman, BSc
N.M. van Sorge, PhD, Professor of Translational Microbiology and Head of the NRLBM
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2 ISOLATES, CSF SPECIMENS AND SERA RECEIVED

The Netherlands Reference Laboratory for Bacterial Meningitis (NRLBM) receives, types and stores isolates cultured from cerebrospinal fluid (CSF) and blood from patients with proven meningitis (CSF and/or blood culture positive), bacteraemia and suspected meningitis (blood culture positive only), and patients with invasive disease with an isolate obtained from a normally-sterile site (Figure 2.1). Unless otherwise indicated, isolates from CSF or CSF and blood are counted as a patient with meningitis, from blood only as a patient with bacteraemia. When CSF is noted as the isolation source, this could indicate an isolate or positive PCR from CSF or CSF and blood. Incidences have been calculated by dividing the number of annually-received isolates (in a particular patient age group) by the number of inhabitants (within that same age group) multiplied by 100,000. Population statistics were obtained from Statistics Netherlands[1] using StatLine using 1 January 2024 as the reference date. By estimation, the NRLBM receives about 90% of the isolates from bacterial meningitis patients in the Netherlands[2].

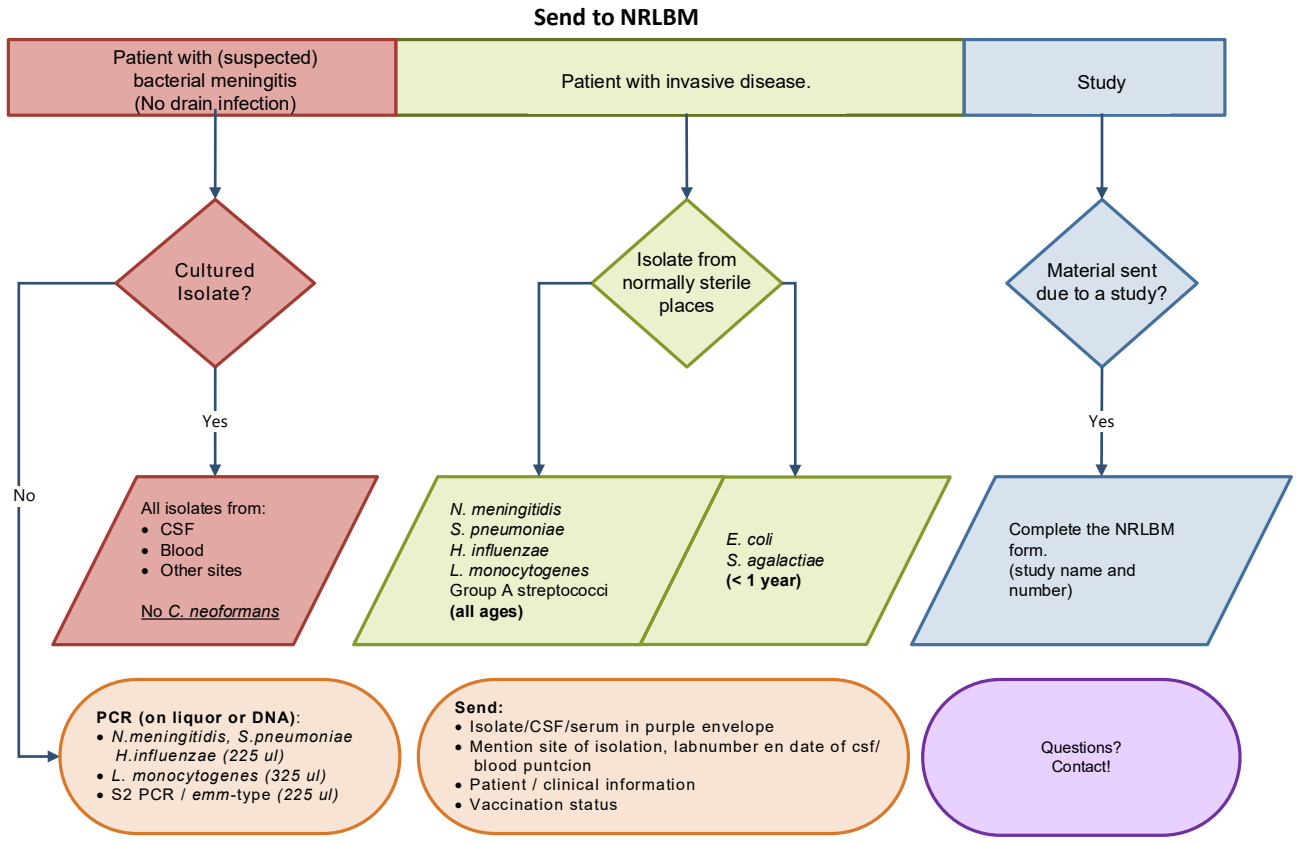


Figure 2.1. *Overview of isolates and materials received by the NRLBM.*

In 2024, the NRLBM received isolates from CSF and/or blood and samples of CSF, serum or other body fluids of 4,834 patients of which 4,750 (98.2%) were cultured or positive in antigen or PCR tests (**table 2.1**). Of all patients, 337 (7.1%) were culture- or PCR-confirmed cases of bacterial meningitis.

[1] CBS - Statline Statistics Netherland www.cbs.nl
[2] Evaluation of the surveillance system for invasive meningococcal disease (IMD) in the Netherlands, 2004–2016; Brandwagt 2019

Table 2.1 Overview of all samples received by the NRLBM in 2024

	Number of specimens
Isolates (all isolation sites; blood/CSF only)	4,691; 2,995
PCR- or antigen-positive samples of CSF, sera and other fluids	59
Total positive isolates and PCR- or antigen-positive samples	**4,750**
PCR- or antigen-negative samples of CSF, sera and other fluids	84
Total	**4,834**

In 2024, 51 clinical microbiology laboratories submitted isolates or samples to the NRLBM. Table 2.2 shows the received isolates or positive PCR samples from 4,750 patients according to the species and laboratory where cases were diagnosed. From 2003 onwards, the NRLBM requested nine sentinel laboratories, evenly distributed across the country and covering (2020-2024) 28% of the Dutch population, to submit pneumococcal isolates from CSF and/or blood from patients of all ages (highlighted in orange Table 2.2). However, population coverage of the sentinel labs has shifted substantially in the past years, due to mergers of diagnostics departments of different hospitals. Therefore, we will report national data based on samples received from all labs from 2024 onwards.

Table 2.2 Number of isolates or PCR-positive samples from CSF and/or blood received in 2024, according to laboratory and bacterial species.

Location	**Laboratory** MM; Medical Microbiology	**Bacterial species#**											
		Nm	Hi	Sp	Ec	Sag	Lm	Spy*	Sau	Cns	Ot	Nv	**Total**
Alkmaar	Northwest Clinics	6	11	59	-	4	-	26	-	-	-	-	**106**
Amersfoort	Meander Medical Center	4	6	55	1	-	4	17	-	-	-	-	**87**
Amsterdam	Amsterdam UMC	4	12	61	10	2	1	35	3	2	11	-	**141**
	OLVG	3	16	68	4	2	4	55	-	-	1	1	**154**
	ATAL medial (Slotervaart / Amstelland)	1	4	14	2	3	1	16	-	-	-	-	**41**
	GG&GD Amsterdam	-	-	-	-	-	-	2	-	-	-	-	**2**
Apeldoorn	Eurofins, MMI Gelre Hospitals	4	7	43	-	1	4	26	-	-	1	-	**86**
Arnhem	Rijnstate Hospital		6	21	1		2	20	-	-	-	-	**50**
Breda	Microvida MMI Brabant & Zeeland	3	9	43	2	2	2	16	-	-		-	**77**
Capelle ad IJssel	IJsselland Hospital	1	1	21	-	2	1	14	-	-	1	-	**41**
Delft	Reinier Haga Medische Diagnostisch Centrum -RHMD	4	2	34	-	2	4	25	-	-	2	-	**73**
Den Bosch	Jeroen Bosch Hospital, MM	5	17	106	1	4	1	41	-	-	2	-	**177**
Den Haag	Haga Hospital	4	5	46	-	2	-	26	-	-	1	-	**84**
	Haaglanden Medical Center	3	8	39	-	1	1	16	-	2	1	-	**71**
Deventer	Deventer Hospital, LMMI	1	9	29	-	1	4	18	-	-	-	-	**62**
Doetinchem	Slingeland Hospital, MM	-	3	17	1	1	-	4	-	-	-	-	**26**
Dordrecht	RLM Dordrecht / Gorinchem	5	4	38	2	1	1	31	-	-	-	-	**82**
Ede	Gelderse Vallei, MM	5	3	33	-	3	-	23	-	-	1	-	**68**
Elst	Dicoon	2	9	60	2	3	2	19			-		**97**
Goes	Microvida MMI Brabant & Zeeland	-	-	26	-	-	1	19	-	-	-	-	**46**
Gouda	Groene Hart Hospital	-	4	22	2	3	-	26	-	-	1	-	**58**

Location	Laboratory MM; Medical Microbiology	Bacterial species#											
		Nm	Hi	Sp	Ec	Sag	Lm	Spy*	Sau	Cns	Ot	Nv	Total
Groningen	Certe, MM	12	17	117	-	1	14	80	2	-	1	-	**244**
	UMCG, MMI	5	7	22	3		3	30	-	-	2	-	**72**
Haarlem	Streeklab voor de Volksgezondheid	7	5	76	-	2	5	45	-	-	-	-	**140**
Harderwijk	St. Jansdal	-	5	31	1	1	-	8	-	-	-	-	**46**
Hengelo	LabMicTa	8	25	104	3	2	9	71	-	-	1	-	**223**
Hilversum	Ter Gooi	1	1	33	-	1	2	27	-	-	1	-	**66**
Hoorn	Comicro, MML	5	7	55	1	1	7	37	-	-	-	-	**113**
Leeuwarden	MCL, Medische Microbiologie	4	15	95	3	3	3	64	-	-	-	-	**187**
Leiden	Eurofins Clinical Diagnostics, Alrijne Hospital	1	2	42	1	2	-	27	-	-	-	-	**75**
	LUMC,MM	1	4	26	6	-	5	10	-	-	1	-	**53**
Maastricht	Maastricht UMC+, MMI&I	1	2	32	1	4	-	25	-	-	-	-	**65**
Nieuwegein	St. Antonius hospital	6	7	74	4	3	1	44	-	-	2	1	**142**
Nijmegen	Canisius Wilhelmina Hospital (CWZ)		4	22	1		1	13	-	-	1	-	**42**
	Radboud UMC	10	15	85	19	1	2	56	-	-	1	-	**189**
Neth Antilles	MM, Aruba/Curacao/St.Maarten	1	6	8	-		2	5	-	-	1	1	**24**
Roermond	Laurentius hospital Roermond (LRZ)	1	1	14	1	2	1	21	-	-	-	-	**41**
Roosendaal	Microvida MMI Brabant & Zeeland, Bravis Hospital	3	6	24	-	1	2	18	-	-	-	-	**54**
Rotterdam	Erasmus MC, MMMI	2	8	28	8	3	4	24	-	-	-	-	**77**
	Ikazia Hospital, MMI	1	2	21	-	2	-	15	-	-	-	-	**41**
	Maasstad Laboratory, Maasstad Hospital	3	8	57	2	2	-	24	1	-	-	-	**97**
	Fransiscus Gasthuis & Vlietland	3	5	59	3	3	-	33	-	-	-	-	**106**
Sittard	Zuyderland Medisch Centrum	3	6	75	-	-	2	29	-	-	-	1	**116**
Terneuzen	Microvida MMI Brabant & Zeeland	2	2	11	-	-	1	6	-	-	-	-	**22**
Tilburg	Microvida MMI Brabant & Zeeland	4	12	68	3	1	2	25	-	-	-	-	**115**
Utrecht	Maatschap MMI, Diaconessenhuis Utrecht	2	6	20	2	1	3	22	-	-	1	-	**57**
	St. Antonius hospital	-	1	-	-		-	2			-	-	**3**
	MMI, UMC Utrecht	2	5	30	16	8	2	32	-	-	-	-	**95**
Veldhoven	Eurofins, PAMM	3	12	41	1	3	4	11	-	-	1	-	**76**
Venlo	Vie Curie Medical Center	-	-	24	-	-	2	22	-	-	-	-	**48**
Zwolle	LMMI, Isala Hospital	1	9	58	2	2	3	46	-	-	-	-	**121**
Total		**147**	**341**	**2187**	**109**	**86**	**113**	**1347**	**6**	**4**	**35**	**4**	**4750**

Nm: *N. meningitidis*; **Hi:** *H. influenzae*; **Sp:** *S. pneumoniae*; **Ec:** *E. coli*; **Sag:** *S. agalactiae*; **Lm:** *L. monocytogenes*; **Spy:** *S. pyogenes*; **Sau:** *S. aureus*; **Cns:** Coagulase-negative staphylococci; **Cn:** *C. neoformans;* **ot:** other bacteria; nv: non viable.
* *S. pyogenes*: NRLBM requests all *S. pyogenes* isolates from patients with invasive group A streptococcal infection, not only meningitis related.

The distribution of the received isolates/samples over the 5-year period 2020-2024 is presented in table 2.3, including only meningitis samples for *S. pyogenes*. For 2024, the top five species are comprised by *S. pneumoniae*, *H. influenzae, N. meningitidis, E. coli, and S. agalactiae*. In 2019, the NRLBM received a total of approximately 2,700 samples. During the COVID-19 years 2020 and 2021 and a part of 2022, the number of samples decreased by 32% on average. This decrease is likely attributable to the introduction of containment policies that

were implemented in response to the COVID-19 pandemic. For 2024, the number of samples (n=3,054) increased compared to 2023 and even exceeded the pre-COVID number of samples from 2019 (~2700).

Table 2.3 Number of isolates from CSF and/or blood received in the years 2020 – 2024

Species[1]	2020			2021			2022			2023			2024		
	CSF	Blood	Total	CSF	Blood	Total	CSF	Blood	Total	CSF	Blood	Total	CSF	Blood	Total
N. meningitidis	27	39	66	19	18	37	41	38	79	59	63	122	66	80	146
H. influenzae	21	181	202	24	143	167	35	287	322	34	280	314	31	310	341
S. pneumoniae	108	1007	1115	87	1030	1117	145	1796	1941	169	2006	2175	156	2031	2187
E. coli	19	75	94	20	80	100	15	77	92	13	90	103	11	98	109
S. agalactiae	22	107	129	19	128	147	21	95	116	13	86	99	9	77	86
L. monocytogenes	11	70	81	12	68	80	10	79	89	14	75	89	20	93	113
S. pyogenes[2,3]	5	1	6	2	1	3	19	8	27	22	10	32	13	10	23
S. aureus	10	0	10	3	0	3	8	0	8	8	0	8	6	0	6
Coag.neg.Staph.	4	1	5	7	0	7	7	0	7	5	0	5	4	0	4
C. neoformans[4]	6	5	11	8	1	9	7	9	16	-	-	-	-	-	-
Others	16	22	38	13	15	28	22	23	45	30	24	54	21	14	35
non viable	0	1	1	0	0	0	0	5	5	0	2	2	-	4	4
Total	**249**	**1509**	**1758**	**214**	**1484**	**1698**	**330**	**2417**	**2747**	**367**	**2636**	**3003**	**337**	**2717**	**3054**

CSF: CSF or CSF and blood / blood: blood only; Non-viable; for 3 *S. pneumoniae* and 1 *H. influenzae* isolates from blood
[1] Including PCR-positive samples
[2] Total 1,347 *S. pyogenes* isolates in 2024; 13 from CSF, 777 blood and 557 non csf/blood isolates; 23 were meningitis related.
[3] *S. pyogenes*; isolates from CSF or from blood with clinical meningitis. All years were corrected for this criteria. In earlier annual reports totals for 2020 and 2021 were higher.
[4] Since januari 2023 *C. neoformans* is no longer sent to NRLBM

The incidence of invasive bacterial infections for the different bacterial species over the years 2020 to 2024 is shown in table 2.4. Incidences follow the number of received isolates/samples, with incidence of invasive pneumococcal disease (IPD; *S. pneumoniae*) returning to pre-COVID19 levels (10.37) and doubling compared to COVID-19 pandemic period. Incidence of invasive meningococcal disease (IMD;*N. meningitidis*) in 2024 is still at lower levels compared to 2019 (0.91), which is likely a result of the introduction of the MenACWY vaccine in 2018 and perhaps still recovery from COVID-19-related restriction. Incidences for invasive *H. influenzae* and *E. coli* increased compared to 2023, whereas incidence of *S. agalactiae* invasive disease showed a declining trend from 2020.

Table 2.4 Incidence of invasive bacterial infections per species per 100,000 inhabitants, 2020 - 2024

Species	2020	2021	2022	2023	2024
N. meningitidis	0.38	0.21	0.45	0.68	0.81
H. influenzae	1.16	0.96	1.83	1.76	1.90
S. pneumoniae	6.41	6.39	11.03	12.21	12.19
E. coli	0.54	0.57	0.52	0.58	0.61
S. agalactiae	0.74	0.84	0.66	0.56	0.48
L. monocytogenes	0.47	0.46	0.51	0.50	0.63
S. pyogenes	0.03	0.02	0.15	0.18	0.13
S. aureus	0.06	0.02	0.05	0.04	0.03
Coag. neg. Staph.	0.03	0.04	0.04	0.03	0.02
C. neoformans	0.06	0.05	0.09	-	-
others	0.22	0.16	0.26	0.30	0.20
non viable	0.01	-	0.03	0.01	0.02
Total	**10.74**	**10.11**	**15.62**	**16.86**	**17.02**

Table 2.5 shows the distribution of isolates according to the source from which they were cultured.

Table 2.5 Total number and proportion of isolates from CSF and/or blood received in 2024, according to bacterial species and source.

Species		CSF or CSF and blood, n	Blood only, n	Total, n	%
Neisseria meningitidis [1]		66	80	146	**4.8**
Haemophilus influenzae [2]		31	310	341	**11.2**
Streptococcus pneumoniae [3]		156	2031	2187	**71.6**
Escherichia coli		11	98	109	**3.6**
Streptococcus agalactiae		9	77	86	**2.8**
Listeria monocytogenes		20	93	113	**3.7**
Streptococcus pyogenes [6]		13	10	23	**0.8**
Staphylococcus aureus		6	0	6	**0.2**
Coagulase-negative staphylococcus [5]		4	0	4	**0.1**
Others total		21	14	35	**1.1**
Others	*Citrobacter koseri*	*1*	*0*	*1*	
	Corynebacterum stratium	*1*	*0*	*1*	
	Enterococcus faecium	*3*	*0*	*3*	
	Indifferent streptococci	*0*	*1*	*1*	
	Klebsiella pneumonia	*1*	*0*	*1*	
	Proteus mirabilis	*1*	*0*	*1*	
	Pseudomonas aeruginosa	*2*	*0*	*2*	
	Rothia mucilaginosa	*1*	*0*	*1*	
	Salmonella species	*1*	*0*	*1*	
	Streptococcus bovis	*1*	*0*	*1*	
	Streptococcus dysgalactiae ssp equisimilis	*1*	*10*	*11*	
	Streptococcus infantis	*1*	*0*	*1*	
	Streptococcus intermedius	*2*	*0*	*2*	
	Streptococcus mitis [4]	*1*	*1*	*2*	
	Streptococcus oralis ssp oralis	*0*	*1*	*1*	
	Streptococcus oralis ssp tigurinus	*1*	*1*	*2*	
	Streptococcus salivarius	*1*	*0*	*1*	
	Streptococcus species	*2*	*0*	*2*	
Non viable		0	4	4	**0.1**
Total		337	2717	3054	**100.0**

1 **In one patient, both *N. meningitidis* and *S. pneumoniae* were isolated from blood within 1 month.**

2 **In nine patients, both *Streptococcus pneumoniae* and *Haemophilus influenzae* were isolated from blood and in two patients, *Streptococcus pneumoniae* was isolated from CSF and *Haemophilus influenzae* from blood (one patient in same episode, other patient one year between isolates).**

3 **In one patient, both *Streptococcus pneumoniae* and *Streptococcus pyogenes* were isolated from blood.**

4 **In one patient, *Streptococcus mitis* and *Streptococcus salivarius* were isolated from CSF**

5 **In one patient, *Staphylococcus epidermidis* and *Enterococcus faecium* *and in another Staphylococcus epidermidis* and *Acetinobacter baumannii* were isolated from CSF**

6 **Meningitis patients only, Total 1,347 S. pyogenes isolates in 2024; 13 from CSF, 777 blood and 557 isolates from other sources; 23 were meningitis related**

3 BACTERIAL MENINGITIS – general overview

In 2024, the NRLBM received CSF isolates or PCR-positive CSF samples from 337 patients (Table 2.3 and 11.1). The proportion of meningococcal, pneumococcal, and haemophilus cases among meningitis patients was 20%, 46%, and 9%, respectively (Figure 3.1). The neonatal pathogens *S. agalactiae* and *E. coli* represented 3% of the meningitis cases each (Figure 3.1)

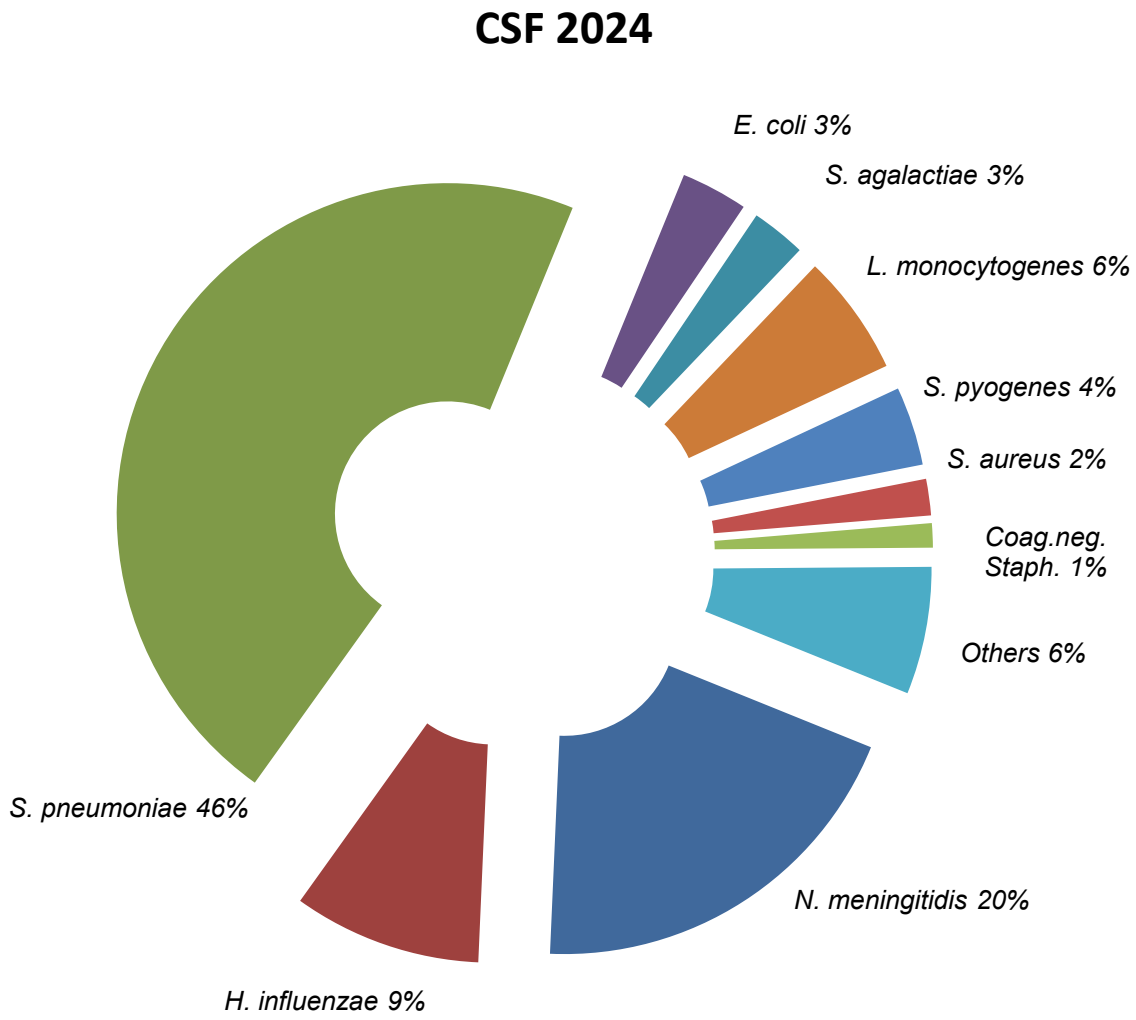


Figure 3.1 *Proportional distribution of CSF isolates and CSF-positive samples according to bacterial species, 2024*

Figure 3.2 shows the total annual number of meningitis cases based onan isolate from CSF and CSF-positive PCRs between 1992-2024. The graph shows a decrease over the last three decades but incidence has stabilized around 2.0 from approximately 2010 until 2023, with a 2-year decreased incidence in 2020 and 2021, associated to the COVID-19 containment measures (Figure 3.2).

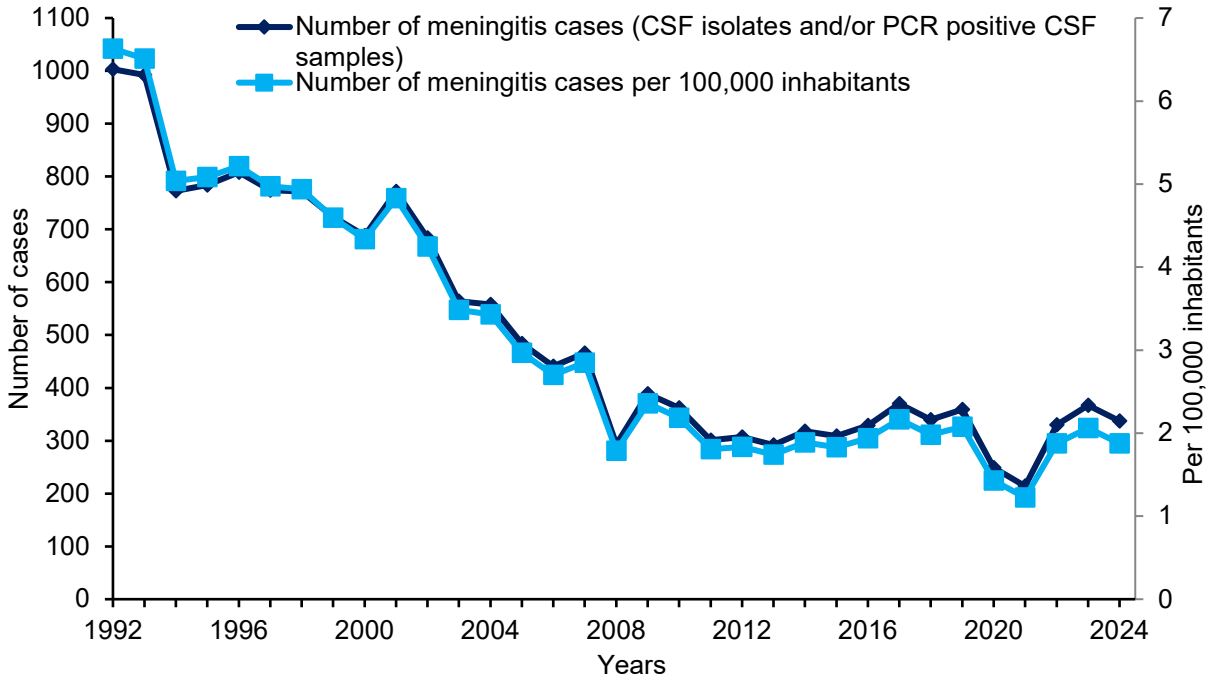


Figure 3.2 *All cause bacterial meningitis cases and incidence, 1992-2024*

Bacterial meningitis cases over the same 30-year period according to specific species, i.e. *N. meningitidis, H. influenzae* and *S. pneumoniae*, are presented in figure 3.3. Comparing meningitis incidence pre- and post-vaccination, the incidence of *Haemophilus* meningitis decreased from 1.6 per 100,000 in 1992 to less than 0.10 in 2009 but increased to 0.20 per 100,000 in 2024. For meningococcal meningitis, the incidence decreased from 3.1/100,000 in 1993 to 0.4/100,000 in 2024. The rapid decline in meningococcal meningitis around 2002 is largely attributed to nationwide vaccination against serogroup C, which started in 2002 and immediately showed an effect in 2003. After an increase in meningococcal meningitis between 2016 and 2018 as a result of a nationwide serogroup W upsurge, the number of meningococcal meningitis cases decreased again to 19 in 2021. This is likely the result of two events; the introduction of the MenACWY vaccine in the National Immunisation Programme as of 1 May 2018 with its catch-up campaign and the COVID-19 containment measures in 2020. Although the incidence of meningococcal meningitis is still low (0.37/100,000/year), the incidence has clearly increased compared to 2020/2021 (0.16/0.11). Pneumococcal meningitis showed a slight increase in annual incidence between 1991 and 2004 from 1.0 to 1.6 per 100,000 inhabitants. The introduction of the 7-valent conjugated polysaccharide vaccine (PCV-7) for children in the National Immunisation Programme in June 2006, and the switch to 10-valent (PCV-10) in 2011, decreased the incidence of pneumococcal meningitis to 0.95 per 100,000 in 2019. In 2020 and 2021, the incidence of pneumococcal meningitis further decreased to 0.6 and 0.50 per 100,000 inhabitants, respectively. Multiple factors are likely to play a role. First of all, the COVID-19 containment measures reduced incidence of several respiratory-transmitted infectious diseases. In addition, for pneumococcal disease, the PPV23 vaccine has been offered to the elderly, starting with the age group 73-79- year-olds (born between 1-1-1941 and 31-12-1947) in autumn 2020, and each consecutive year by the following birth cohorts: 2021: 1948-1953, 2022: 1953-1956, 2023: 1956-1961, 2024: 1961-1964. Finally, in the pediatric vaccination program, PCV10 has been replaced by PCV15 from September 2024. All these changes in vaccination schedules are likely to affect the incidence of pneumococcal meningitis.

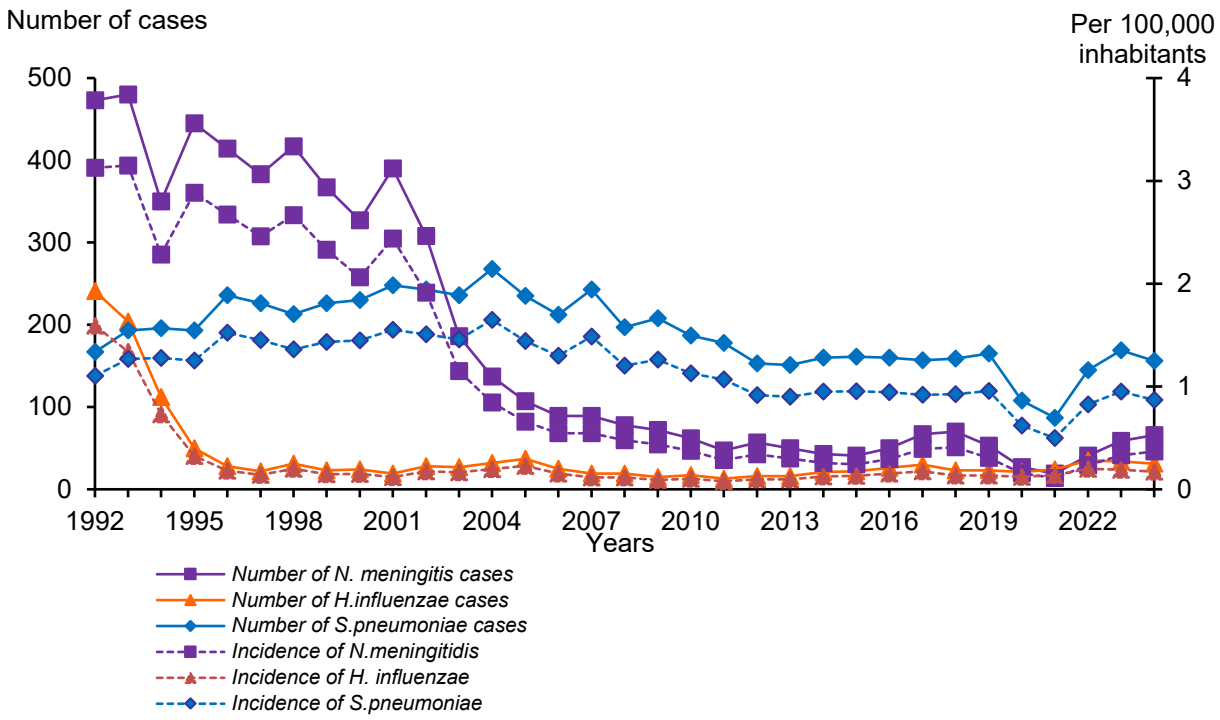


Figure 3.3 *Number of cases and incidence (per 100,000 inhabitants) of meningococcal, haemophilus and pneumococcal meningitis (isolates and/or positive PCR from CSF), 1992-2024*

Table 3.1 shows the number of CSF isolates and/or CSF-positive PCRs by annual quarter grouped by bacterial species. Most isolates/samples were received in Q1 2024.

Table 3.1 Isolates and PCR-positive samples from CSF by annual quarter according to bacterial species, 2024

	ANNUAL QUARTER					
SPECIES	**First**	**Second**	**Third**	**Fourth**	**Total**	**%**
N. meningitidis	26	16	12	12	**66**	***19.6***
H. influenzae	13	9	4	5	**31**	***9.2***
S. pneumoniae	56	37	17	46	**156**	***46.3***
E. coli	4	2	1	4	**11**	***3.2***
S. agalactiae	2	4	2	1	**9**	***2.7***
L. monocytogenes	5	4	4	7	**20**	***5.9***
S. pyogenes	8	3	2	0	**13**	***3.9***
S. aureus	1	0	2	3	**6**	***1.8***
Coag.neg.Staph.	0	2	0	2	**4**	***1.2***
Others	6	7	3	5	**21**	***6.2***
non viable	0	0	0	0	**0**	***0***
Total	**121**	**84**	**47**	**85**	**337**	***100.0***
%	***35.9***	***24.9***	***13.9***	***25.2***	***100.0***	

Table 3.2 shows the distribution of culture and non-culture positive CSF samples according to bacterial species and patient age. Table 3.3 shows the age-specific incidence per 100,000 individuals for the same samples. *S. agalactiae* and *E. coli* are still the predominant species isolated from neonates (i.e. younger than 1 month; Table 3.2), and together represented 71%

of all isolates in this age group. In contrast, in infants 1-11 months of age, *S. pneumoniae* caused 36% of meningitis cases, followed by *N. meningitidis* (27%), *H. influenzae* (15%), *E. coli* (9%) and *S. agalactiae* (6%). Since the introduction of the *H. influenzae* b vaccine in 1993, the number of *H. influenzae* b meningitis cases in the age group 0-4 year has strongly decreased, from 231 in 1992 to 11 in 2024 (Table 3.2). Overall, for children ages 0-4 years, *S. pneumoniae* and *N. meningitidis* were the predominant cause of bacterial meningitis, representing 27% and 25%, respectively, of all meningitis cases in this age group. *S. pneumoniae* is also the predominant cause of meningitis among patients 50+ years of age, with 59% of all cases.

Table 3.2 Isolates/PCR-positive samples from CSF grouped according to species and age, 2024

	AGE (MONTHS)			AGE (YEARS)									TOTAL
Group	**0**	**1-11**	**12-59**	**0-4**	**5-9**	**10-14**	**15-19**	**20-29**	**30-39**	**40-49**	**50-64**	**65-79**	**≥80**	**Total, n**
N. meningitidis	0	9	8	17	3	2	11	12	4	4	12	0	1	**66**
H. influenzae	0	5	6	11	2	0	0	1	0	2	8	5	2	31
S. pneumoniae	1	12	6	19	5	3	3	2	11	20	46	37	10	156
E. coli	5	3	0	8	0	0	0	0	0	1	1	1	0	11
S. agalactiae	5	2	0	7	0	0	0	0	0	0	1	1	0	9
L. monocytogenes	1	1	0	2	0	0	0	0	1	1	3	13	0	20
S. pyogenes	0	0	0	0	2	2	1	1	2	2	2	1	0	13
S. aureus	0	0	0	0	0	0	0	0	1	3	1	1	0	6
Coag.neg.Staph.	1	0	0	1	0	0	0	1	0	1	1	0	0	4
Others	1	1	2	4	1	0	2	1	1	2	4	4	2	21
non viable	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total, n	*14*	*33*	*22*	*69*	*13*	*7*	*17*	*18*	*20*	*36*	*79*	*63*	*15*	337
%	***4.2***	***9.8***	***6.5***	***20.5***	***3.9***	***2.1***	***5.0***	***5.3***	***5.9***	***10.7***	***23.4***	***18.7***	***4.5***	***100***

As observed in table 3.2, the incidence of all-cause bacterial meningitis was highest in the 0-11 month age group (table 3.3) with 47 cases per 100,000. The overall incidence of bacterial meningitis decreased to the level of 2022, wich was also 1.88 (figure 3.2).

Table 3.3 Age-specific incidence of bacterial meningitis per 100,000 inhabitants, 2024

	AGE (YEARS)										
SPECIES	**0**	**1-4**	**5-9**	**10-14**	**15-19**	**20-29**	**30-39**	**40-49**	**50-64**	**65-79**	**≥80**	Total
N. meningitidis	5.47	1.14	0.33	0.21	1.08	0.51	0.17	0.19	0.32	-	0.11	0.37
H. influenzae	3.04	0.86	0.22	-	-	0.04	-	0.09	0.22	0.18	0.22	0.17
S. pneumoniae	7.90	0.86	0.56	0.32	0.29	0.08	0.47	0.94	1.24	1.33	1.11	0.87
E. coli	4.86	-	-	-	-	-	-	0.05	0.03	0.04	-	0.06
S. agalactiae	4.26	-	-	-	-	-	-	-	0.03	0.04	-	0.05
L. monocytogenes	1.22	-	-	-	-	-	0.04	0.05	0.08	0.47	-	0.11
S. pyogenes	-	-	0.22	0.21	0.10	0.04	0.09	0.09	0.05	0.04	-	0.07
S. aureus	-	-	-	-	-	-	0.04	0.14	0.03	0.04	-	0.03
Coag.neg.Staph.	0.61	-	-	-	-	0.04	-	0.05	0.03	-	-	0.02
Others	1.22	0.29	0.11	-	0.20	0.04	0.04	0.09	0.11	0.14	0.22	0.12
non viable	-	-	-	-	-	-	-	-	-	-	-	-
Total	**28.58**	**3.15**	**1.45**	**0.47**	**1.67**	**0.76**	**0.85**	**1.69**	**2.13**	**2.27**	**1.67**	**1.88**

Table 3.4 shows the number of CSF isolates per species according to patient sex. Overall, the Male/Female ratio was around 1, except for *S. pneumoniae, S. agalactiae,* and *S. aureus*, which affected males more often than females.

Table 3.4 Isolates and PCR-positive samples from CSF according to patients' sex, 2024

SPECIES	M	F	M/F – ratio	Sex not known	Total
N. meningitidis	31	35	**0.9**	-	**66**
H. influenzae	14	17	**0.8**	-	**31**
S. pneumoniae	88	68	**1.3**	-	**156**
E. coli	5	6	**0.8**	-	**11**
S. agalactiae	6	3	**2.0**	-	**9**
L. monocytogenes	11	9	**1.2**	-	**20**
S. pyogenes	6	7	**0.9**	-	**13**
S. aureus	5	1	**5.0**	-	**6**
Coag.neg.Staph.	2	2	**1.0**	-	**4**
Others	9	12	**0.8**	-	**21**
Total	**177**	**160**	**1.1**	**-**	**337**
%	***52.5***	***47.5***		**-**	***100***

4 NEISSERIA MENINGITIDIS

4.1 General features

In 2024, the NRLBM received 110 *Neisseria meningitidis* isolates of which 34 were isolated from CSF (or CSF and blood; 26 in 2023) and 76 from blood only (62 in 2023). In addition, 36 culture-negative CSF/blood samples tested positive for meningococci by PCR bringing the total number of received meningococcal isolates or PCR-positive samples to 146. The distribution of isolates received throughout the year followed the common seasonal pattern. The highest number of isolates/positive-samples was received in Q1 of 2024 (figure 4.1).

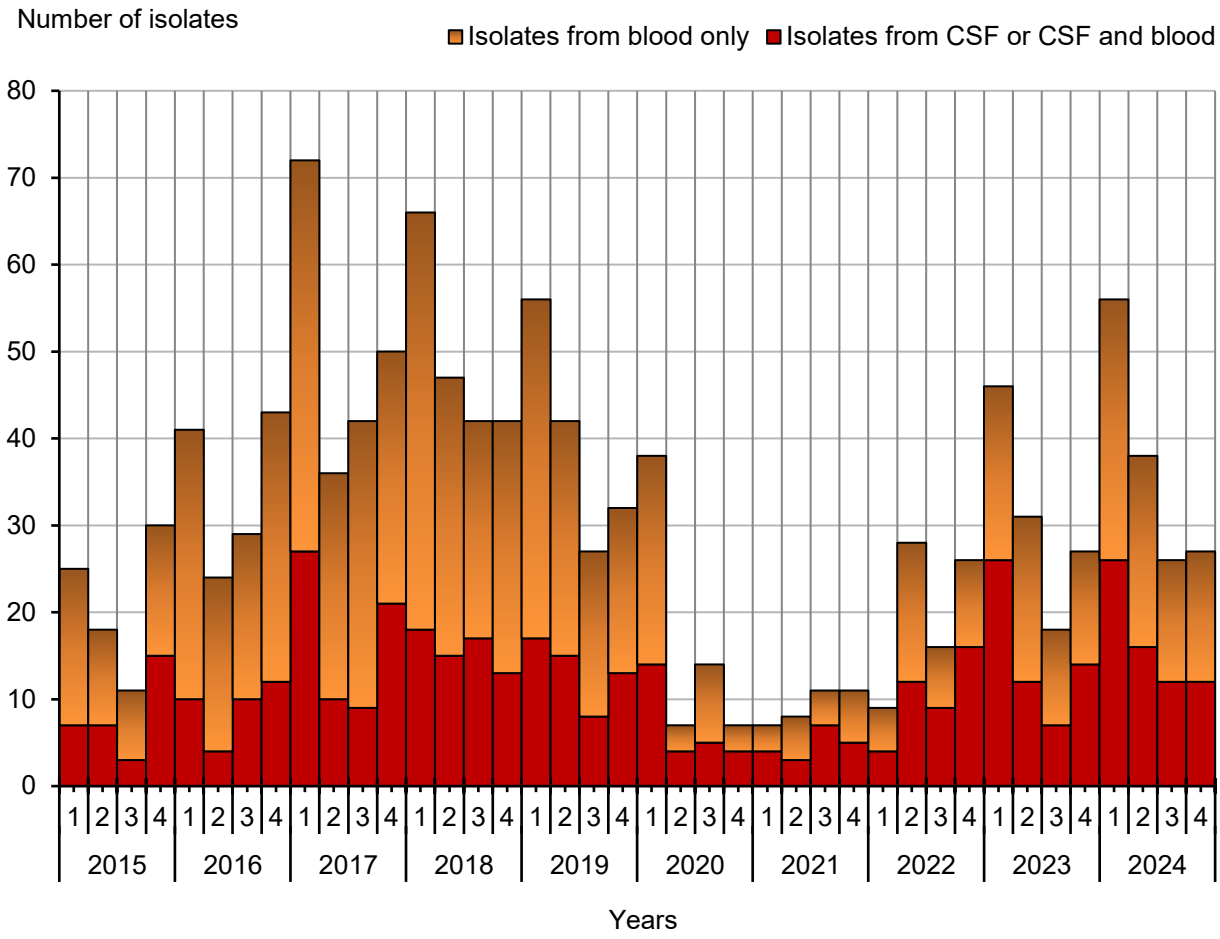


Figure 4.1 *Seasonal distribution of received meningococcal samples (culture or PCR-positive CSF or blood samples), 2015-2024*

4.2 Antibiotic susceptibility

Nearly all isolates (107/110; 97%) were susceptible to penicillin according to the current EUCAST break point (MIC ≤ 0.25 µg/ml is susceptible; Table 4.1). In general, meningococcal resistance to penicillin is rare in the Netherlands (Tables 4.2, 4.3).

Table 4.1 Penicillin susceptibility of all received *N. meningitidis* isolates according to source of isolation (CSF and/or blood), 2024

Penicillin*				
	MIC ≤ 0.25 (S)	**MIC>0.25 (R)**	**Total**	**%**
CSF or CSF and blood	33	1	**34**	***31***
Blood only	74	2	**76**	***69***
Total	**107**	**3**	**110**	***100***
%	***97***	***3***	***100***	

* MIC values in µg/ml

Table 4.2 Penicillin susceptibility of *N. meningitidis* isolates from CSF, 2020-2024

Penicillin*					
	MIC ≤ 0.25 (S)		**MIC>0.25 (R)**		**Total**
	N	%	N	%	
2020	14	*93*	1	*7*	**15**
2021	*7*	*100*	0	*0*	**7**
2022	18	*100*	0	*0*	**18**
2023	26	*100*	0	*0*	**26**
2024	**33**	*97*	1	*3*	**34**

* MIC values in µg/ml

Table 4.3 Penicillin susceptibility of *N. meningitidis* isolates from blood only, 2020-2024

Penicillin*					
	MIC ≤ 0.25 (S)		**MIC>0.25 (R)**		**Total**
	N	%	N	%	
2020	39	*100*	0	*0*	39
2021	18	*100*	0	*0*	18
2022	38	*100*	0	*0*	38
2023	60	*97*	2	*3*	62
2024	74	*97*	2	*3*	76

* MIC values in mg/L

4.3 Serogroups

Serogroup B accounted for 88% (n=128) of all received isolates / PCR-positive samples (Table 4.4), which is an increase in absolute numbers and a very small increase in proportion compared to previous year (2023 85%; 2022 87%; 2021 84%; 2020 61%). The proportion of serogroup W isolates decreased to 5% (table 4.4) compared to 7% in 2023, and compared to previous years (18% in 2020 and 50% in 2018; figure 4.2). In absolute numbers, the NRLBM received fewer serogroup W isolates (n = 7) compared to the previous three years (2019-2021) (Figure 4.2). This reduction in meningococcal W cases is likely a result from the (catch-up) vaccination campains with MenACWY in the National Immunisation Programme as of 1 May 2018. The MenACWY vaccine was introduced to the vaccination program to counter an outbreak of meningococcal W between 2016-2018 and replaced the MenC vaccine.

Serogroup X, Y, E and Non Groupable (NG) meningococci were responsible for 4.8% (together n=7) of all cases of IMD in 2024 (Table 4.4). In 2024, 4 serogroup C were received, all isolated from blood. Both the proportion as well as absolute number of serogroup C isolates increased between 1991 and 2001 from approximately 10% in 1994 (66 cases) to 19% (105 cases) in 2000 and 40% (276 cases) in 2001 (Figure 4.2). After implementation of the serogroup C vaccine in the National Immunisation Program in June 2002, a rapid decline and near eradication of MenC disease was observed.(Figure 4.2)

Overall, serogroups B has the highest incidence of IMD, with the other serogroups represented nearly equally and all below 0.05/100,000 cases for the remaining cases (Table 4.4). The geographical distribution of IMD across the Netherlands is displayed in Figure 4.3.

Table 4.4 Number of meningococci (Incidence of meningococcemia per 100,000 inhabitants) according to serogroup and source of isolation, 2024

Source	Serogroup (inc) B	C	W	Y	X	E	NG*	Total, n
CSF	63 (0.35)	0 (0.00)	2 (0.01)	0 (0.00)	0 (0.00)	0 (0.00)	1 (0.01)	66 (0.37)
Blood[1]	65 (0.36)	4 (0.03)	5 (0.03)	2 (0.01)	2 (0.01)	1 (0.01)	1 (0.01)	80 (0.45)
Total	**128 (0.71)**	**4 (0.03)**	**7 (0.04)**	**2 (0.01)**	**2 (0.01)**	**1 (0.01)**	**2 (0.01)**	**146 (0.82)**
%	**87.6**	**2.7**	**4.8**	**1.4**	**1.4**	**0.7**	**1.4**	**100**

*Non groupable; in PCR not A, B, C, W, Y

[1] Blood; isolates from blood

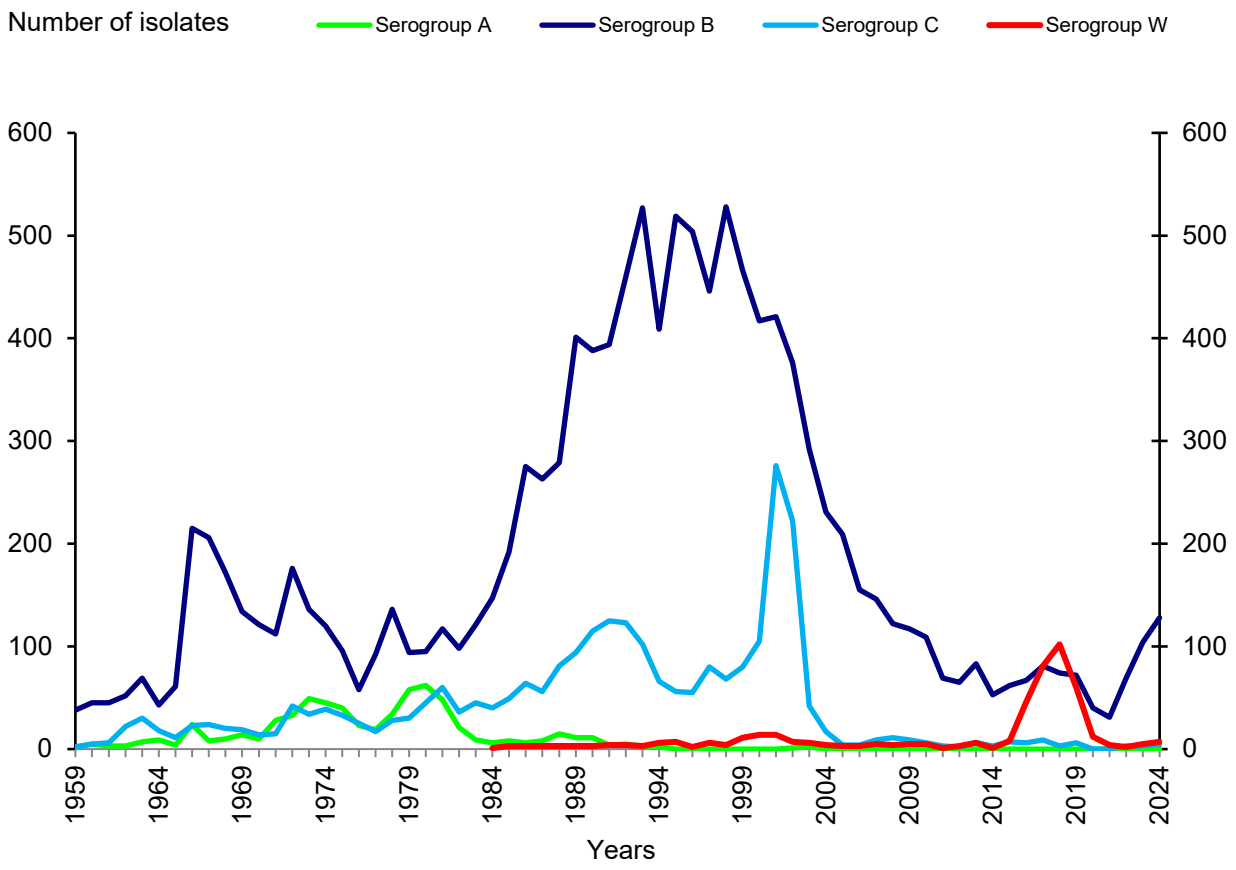
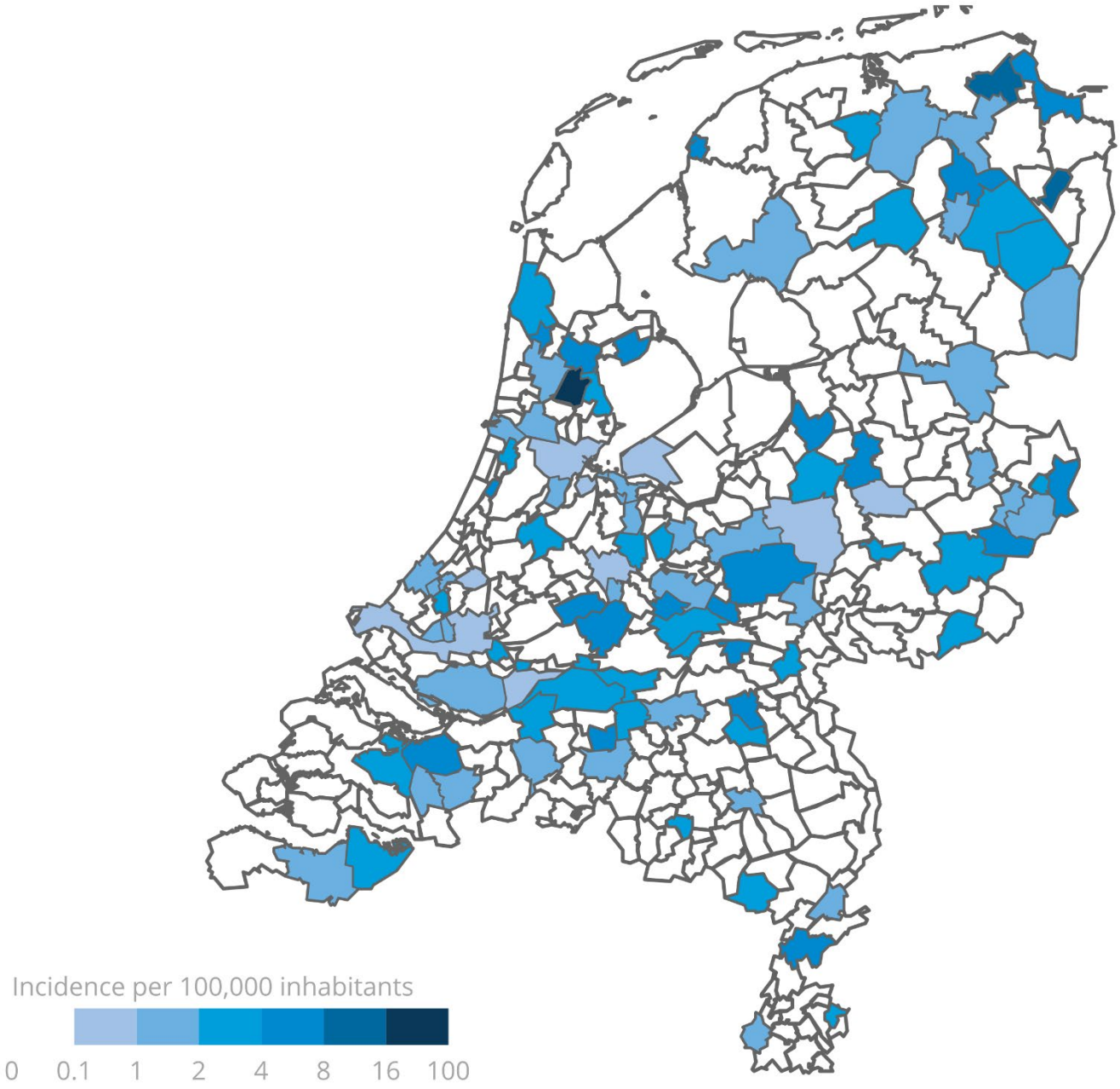


Figure 4.2. *Distribution of meningococcal serogroups A, B, C and W from 1959-2024.*

Figure 4.3 Geographical distribution of *N. meningitidis* (CSF and/or blood) cases based on incidence, *2024*. Incidence is calculated per municipality based on patient's place of residence.



4.4 Serogroup and age

Among MenB cases, 29% (37 of 128) of patients was below the age of 5 years and 62% (79/128) was between 0 and 25 years of age (table 4.6). Almost half (49%) of serogroup B isolates (63/128) were cultured from CSF, whereas the other encapsulated meningococci were predominantly isolated from blood (2 MenW and 1 Non Groupable isolate). This suggests that the clinical presentation and population at risk for infection may be different for serogroup B versus C, W, Y, X and E meningococci. Overall, the incidence of IMD is highest in the age groups < 1 year, 1-4 years and 15-19 years of age with dominant contribution of serogroup B (table 4.7). Currently, the available MenB vaccines (Bexsero and Trumemba) are not included in the National Immunisation Programme.[3]

Table 4.6 Serogroups of *N. meningitidis* (isolates or PCR-positive samples from CSF and /or blood; absolute numbers) according to patient's age and isolation source, 2024

	AGE (MONTHS)			AGE (YEARS)									TOTAL	
Group	0	1-11	12-59	0-4	5-9	10-14	15-19	20-24	25-29	30-49	50-64	≥65	n	%
B	**1**	**16**	**20**	**37**	**7**	**3**	**19**	**13**	**8**	**10**	**18**	**13**	**128**	***87.6***
CSF	*0*	*8*	*8*	*16*	*3*	*2*	*11*	*5*	*7*	*7*	*11*	*1*	*63*	*43.1*
Blood	*1*	*8*	*12*	*21*	*4*	*1*	*8*	*8*	*1*	*3*	*7*	*12*	*65*	*44.5*
C	**0**	**0**	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**0**	**0**	**3**	**4**	***2.7***
CSF	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Blood	*0*	*0*	*0*	*0*	*0*	*1*	*0*	*0*	*0*	*0*	*0*	*3*	*4*	*2.7*
W	**0**	**1**	**2**	**3**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**2**	**7**	***4.8***
CSF	*0*	*1*	*0*	*1*	*0*	*0*	*0*	*0*	*0*	*0*	*1*	*0*	*2*	*1.4*
Blood	*0*	*0*	*2*	*2*	*0*	*0*	*1*	*0*	*0*	*0*	*0*	*2*	*5*	*3.4*
Y	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**2**	***1.4***
CSF	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Blood	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*1*	*1*	*2*	*1.4*
E	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	***0.7***
CSF	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Blood	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*1*	*1*	*0.7*
X	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**0**	**0**	**0**	**0**	**2**	***1.4***
CSF	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Blood	*0*	*0*	*0*	*0*	*0*	*0*	*1*	*1*	*0*	*0*	*0*	*0*	*2*	*1.4*
NG*	**0**	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**0**	**1**	**0**	**0**	**2**	***1.4***
CSF	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*1*	*0*	*0*	*1*	*0.7*
Blood	*0*	*0*	*0*	*0*	*1*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*1*	*0.7*
Total	**1**	**17**	**22**	**40**	**8**	**4**	**21**	**14**	**8**	**11**	**20**	**20**	**146**	***100.0***
CSF	*0*	*9*	*8*	***17***	***3***	***2***	***11***	***5***	***7***	***8***	***12***	***1***	***66***	***45.2***
Blood	*1*	*8*	*14*	***23***	***5***	***2***	***10***	***9***	***1***	***3***	***8***	***19***	***80***	***54.8***
%	***0.7***	***11.6***	***15.1***	***27.4***	***5.5***	***2.7***	***14.4***	***9.6***	***5.5***	***7.5***	***13.7***	***13.7***		***100.0***

*One isolate from blood, NG; One CSF sample, no reaction with ABCYW in serogroup PCR

[3] Gezondheidsraad. Vaccinatie tegen meningokokken. Den Haag: Gezondheidsraad, 2025
https://www.rijksoverheid.nl/documenten/publicaties/2025/02/21/werkagenda-advisering-vaccinaties-gezondheidsraad-februari-2025
Werkagenda advisering Vaccinaties Gezondheidsraad 2025 | Publicatie | Rijksoverheid.nl

Table 4.7 Incidence of invasive meningococcal disease per 100,000 inhabitants according to meningococcal serogroup and patient's age, 2024

	AGE (YEARS)										TOTAL
Group	**0**	**1-4**	**5-9**	**10-14**	**15-19**	**20-24**	**25-29**	**30-49**	**50-64**	**≥65**	
B	**10.34**	**2.86**	**0.78**	**0.32**	**1.86**	**1.10**	**0.68**	**0.22**	**0.49**	**0.35**	**0.71**
CSF	*4.86*	*1.14*	*0.33*	*0.21*	*1.08*	*0.42*	*0.60*	*0.16*	*0.30*	*0.03*	***0.35***
Blood	*5.47*	*1.72*	*0.45*	*0.11*	*0.78*	*0.68*	*0.09*	*0.07*	*0.19*	*0.33*	***0.36***
A,C,Y,W	**0.61**	**0.29**	**0**	**0.21**	**0.10**	**0**	**0**	**0**	**0.05**	**0.16**	**0.08**
CSF	*0.61*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0.03*	*0*	***0.01***
Blood	*0*	*0.29*	*0*	*0.21*	*0.10*	*0*	*0*	*0*	*0.03*	*0.16*	***0.07***
E,X,NG	**0**	**0**	**0.11**	**0**	**0.10**	**0.08**	**0**	**0.02**	**0**	**0.03**	**0.03**
CSF	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0.02*	*0*	*0*	***0.01***
Blood	*0*	*0*	*0.11*	*0*	*0.10*	*0.08*	*0*	*0*	*0*	*0.03*	***0.02***
Total	**10.94**	**3.15**	**0.89**	**0.53**	**2.06**	**1.18**	**0.68**	**0.25**	**0.54**	**0.54**	**0.82**
CSF	***5.47***	***1.14***	***0.33***	***0.21***	***1.08***	***0.42***	***0.60***	***0.18***	***0.32***	***0.03***	***0.37***
Blood	***5.47***	***2.00***	***0.56***	***0.32***	***0.98***	***0.76***	***0.09***	***0.07***	***0.22***	***0.52***	***0.45***

Figure 4.5 shows the age distribution of patients with IMD caused by serogroup B. The age-specific incidence for MenB per 100,000 inhabitants in the age groups 0-4 years of age and 15 - 19 years years of age was 4.3 and 1.9, respectively (Figure 4.5B and Table 4.7).

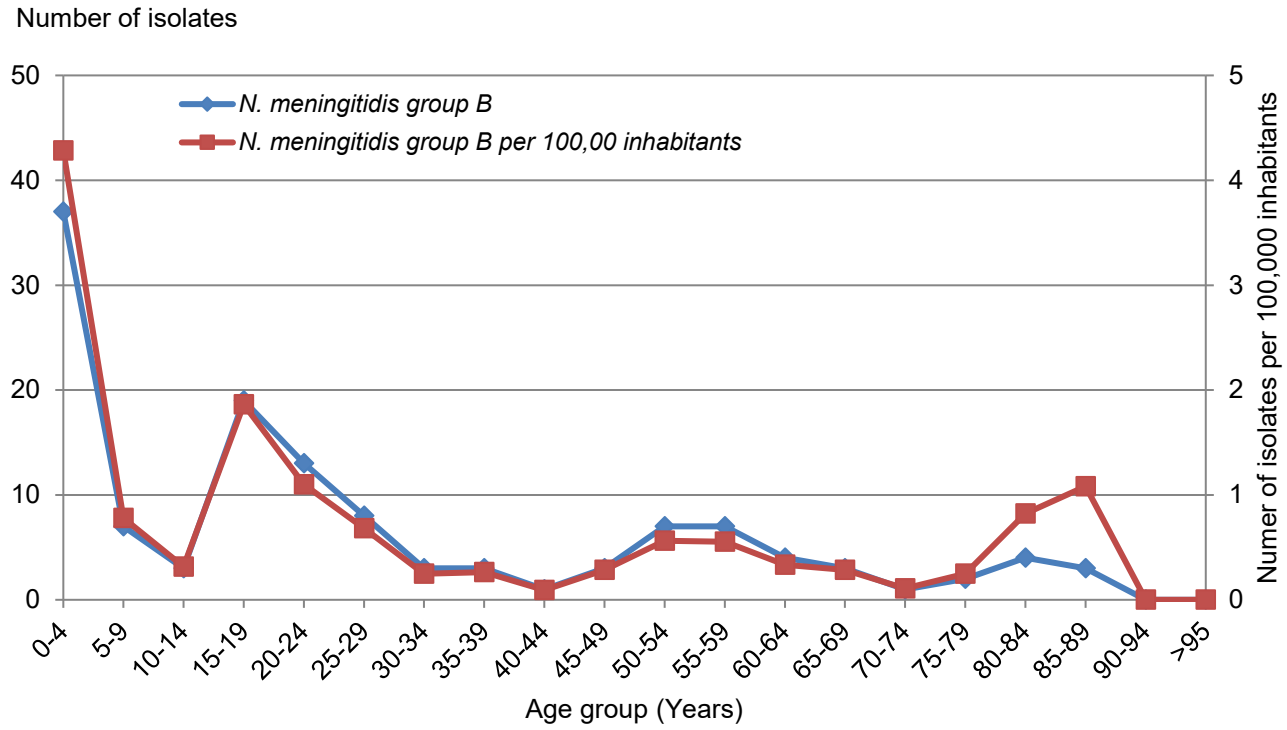


Figure 4.5 *Number of isolates and incidence of meningococcal disease* per 100,000 inhabitants *caused by serogroup B according to age groups, 2024*

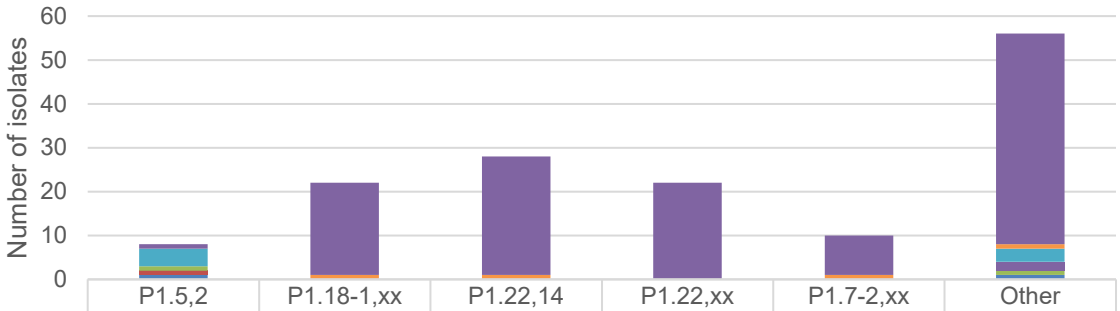
4.5 Distribution of PorA and FetA genosubtypes among meningococci

4.5.1 PorA

In addition to serogrouping, meningococci can be further subtyped based on the variation in PorA and FetA proteins. From January 1, 2005, the NRLBM replaced antibody-based subtyping of PorA and FetA with molecular methods, i.e. DNA-sequencing of PorA and FetA DNA coding regions, due to discontinuation of monoclonal antibodies required for typing.

The PorA epitopes that react with the monoclonal antibodies of the subtyping scheme are encoded by the *porA* variable regions VR1 and VR2, which are now routinely determined by Sanger sequencing for all meningococcal isolates. The DNA sequences are translated into putative amino acid sequences and compared with *porA* epitopes present in the PubMLST database https://pubmlst.org/neisseria/PorA/ PubMLST – PorA typing[4]) (PubMLST - PorA typing, sd). As an example for a PorA notation, (VR1,VR2): P1.7,4, in which VR1 is P1.7 indicates the VR1 region and the second P1.4 indicates the VR2 region, resulting in the combination P1.7,4.

In 2024, the NRLBM received 110 isolates and 36 PCR-positive samples. Of the culture-negative PCR-positive samples, 23 (64%) could be completely subtyped whereas the remaining 13 could not be or were incompletely subtyped. Overall, 38 different VR1/VR2 combinations were encountered among 128 serogroup B meningococci (2023: 40 different combinations; 2022: 24 different combinations; 2021: 16 different combinations). The proportion of dominant *porA* genosubtypes has shifted tremendously in the last two decades: in 2000, genosubtype P1.7-2.4 represented 40% of all serogroup B isolates and gradually declined to only 4.7% in 2024 (table 4.8). In 2024, P1.22,14 was the most abundant genosubtype with 27 out of 128 isolates (21%; Figure 4.6). P1.22 represents 38% of the genosubtypes (49/128).



	P1.5,2	P1.18-1,xx	P1.22,14	P1.22,xx	P1.7-2,xx	Other
B	1	21	27	22	9	48
C		1	1		1	1
W	4					3
Y						2
X	1					1
E	1					
NG	1					1

Figure 4.6 *Distribution of PorA genosubtypes among all received meningococcal cases, 2024*

[4] *PubMLST - PorA typing*. Public databases for molecular typing: https://pubmlst.org/neisseria/PorA/

Table 4.8 PorA genosubtype distribution of *N. meningitidis* serogroup B isolates from 2020-2024 and hypothetical coverage by NonaMen vaccine.

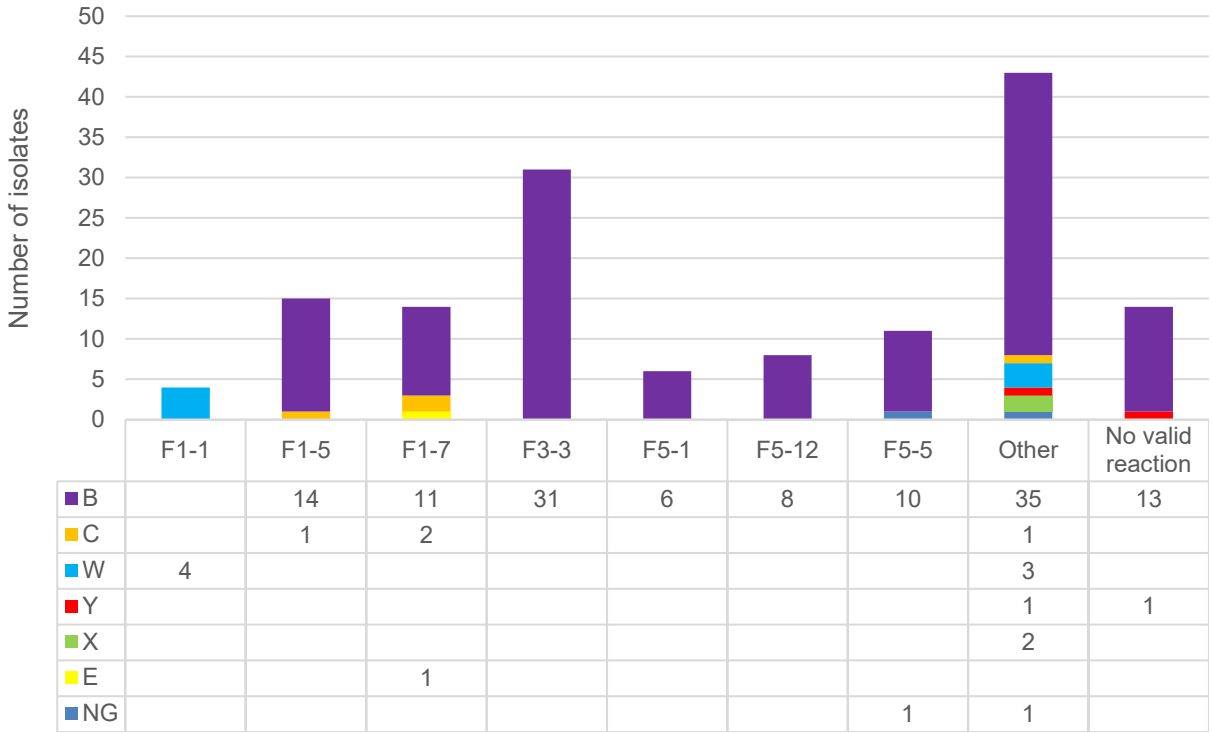
	VR1.VR2 combination	YEAR									
		2020		2021		2022		2023		2024	
		No.	%	No.	%	No.	%	No.	%	No.	%
Vaccine types*	1.5-1, 2-2	1	**2.5**	0	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**
	1.5-1, other	0	**0.0**	0	**0.0**	2	**2.9**	2	**1.9**	0	**0.0**
	Other, 2-2	0	**0.0**	0	**0.0**	1	**1.5**	0	**0.0**	0	**0.0**
	1.5-2,10	0	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**	1	**0.8**
	1.5-2, other	2	**5.0**	0	**0.0**	0	**0.0**	5	**4.8**	3	**2.3**
	Other,10	0	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**
	1.7,16	1	**2.5**	0	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**
	1.7, other	3	**7.5**	1	**3.2**	0	**0.0**	2	**1.9**	1	**0.8**
	Other, 16	1	**2.5**	0	**0.0**	2	**2.9**	3	**2.9**	4	**3.1**
	1.7-1, 1	1	**2.5**	0	**0.0**	3	**4.3**	3	**2.9**	5	**3.9**
	1.7-1, other	0	**0.0**	0	**0.0**	0	**0.0**	1	**1.0**	0	**0.0**
	Other, 1	1	**2.5**	0	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**
	1.7-2,4	4	**10.0**	3	**9.7**	1	**1.5**	7	**6.7**	6	**4.7**
	1.7-2, other	5	**12.5**	3	**9.7**	2	**2.9**	1	**1.0**	3	**2.3**
	Other 4	0	**0.0**	1	**3.2**	0	**0.0**	0	**0.0**	1	**0.8**
	1.12-1,13	0	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**
	1.12-1, other	1	**2.5**	0	**0.0**	3	**4.3**	2	**1.9**	8	**6.3**
	Other, 13	0	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**	1	**0.8**
	1.18-1,3	0	**0.0**	0	**0.0**	0	**0.0**	1	**1.0**	0	**0.0**
	1.18-1, other	2	**5.0**	3	**9.7**	13	**18.8**	13	**12.5**	21	**16.4**
	Other, 3	1	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**
	1.19,15-1	1	**2.5**	0	**0.0**	0	**0.0**	2	**1.9**	4	**3.1**
	1.19, other	3	**7.5**	1	**3.2**	2	**2.9**	2	**1.9**	3	**2.3**
	Other, 15-1	0	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**
	1.22,14	2	**5.0**	10	**32.3**	19	**27.5**	28	**26.9**	27	**21.1**
	1.22,other	7	**17.5**	4	**12.9**	12	**17.4**	21	**20.2**	22	**17.2**
	Other, 14	0	**0.0**	1	**3.2**	1	**1.5**	1	**1.0**	1	**0.8**
	Subtotal vaccine types	36	**90.0**	27	**87.1**	61	**88.4**	94	**90.4**	111	**86.7**
NVT**	Other **Non Vaccine Type**	4	**10.0**	4	**12.9**	8	**11.6**	10	**9.6**	17	**13.3**
	Total	72	**100.0**	40	**100.0**	31	**100.0**	69	**100.0**	128	**100.0**

4.5.2 FetA

In addition to *porA* epitope sequencing, meningococcal isolates/samples are also characterized by *fetA* epitope sequencing, which encodes the outer membrane protein FetA and is considered as a potential vaccine component. Therefore, the variability of this protein has been investigated intensively. The most variable part of the protein, called VR, has been used to establish a typing scheme. Analogous to *porA* typing, the VR part of *fetA* is Sanger sequenced and translated to a putative amino acid sequence. So far, approximately 270 VR sequences comprising 6 classes are identified, which are available at https://pubmlst.org/neisseria/FetA/. (PubMLST)[5]. As an example of a type designation: F5-2, in which the first digit indicates the class and the second digit the variant within this class.

In 2024, 22 different *fetA* variants were observed among 128 serogroup B meningococci, among which F3-3 (24%), F1-5 (11%) and F5-5 (9%) were the three dominant types (figure 4.7; table 4.9). In previous years, F1-5 constituted the dominant type within serogroup B meningococci (table 4.9), with strong linkage to *porA* VR1/VR2 P1.7-2,4. Together, these types linked to the MLST clonal complex ST41/44. In 2024, 14 isolates were of *fetA* type F1-5, of which four were linked to P1.7-2,4 and 10 were linked to different *porA* types. In total, 38 different *porA* VR1/VR2 combinations and 22 different *fetA* variants were encountered among serogroup B meningococci. In 2024, frequently found combinations were P1.22,14:F5-5 (6%) and P1.22,9:F1-55 (5%).

In 2024, we received 7 serogroup W samples, 2 from CSF and 3 from blood. The 7 meningococcal serogroup W isolates displayed 3 different *fetA* types F1-1, F1-66 and F5-8 (Figure 4.7, Table 4.9). Four F1-1 types were linked to *porA* VR1/VR2 P1.5,2 and MLST clonal complex 11.



	F1-1	F1-5	F1-7	F3-3	F5-1	F5-12	F5-5	Other	No valid reaction
B		14	11	31	6	8	10	35	13
C		1	2					1	
W	4							3	
Y								1	1
X								2	
E			1						
NG							1	1	

Figure 4.7 *Distribution of meningococcal* fetA *genosubtypes, 2024*

5
PubMLST - FetA variable region typing. Public databases for molecular typing: https://pubmlst.org/neisseria/FetA/

Table 4.9 % distribution in *fetA* genosubtype among *N. meningitidis* serogroups B, C and W isolates, 2019*(only for McW) 2020-2024

	% Men B					% Men C					% Men W					
Years / FetA	2020	2021	2022	2023	2024	2020	2021	2022	2023	2024	2019	2020	2021	2022	2023	2024
F1-1	0	0	0	0	0	0	0	0	0	0	**88**	**100**	50	50	80	57
F1-5	13	16	10	8	11	0	0	0	33	25	**3**	**0**	0	0	0	0
F1-7	3	6	6	9	9	0	0	67	0	50	**0**	**0**	0	0	0	0
F1-55	0	0	3	4	5	0	0	0	0	0	**0**	**0**	0	0	0	0
F1-66	0	0	3	1	5	0	0	0	0	0	**0**	**0**	0	0	0	14
F3-3	18	13	25	17	24	0	0	0	0	0	**0**	**0**	0	0	0	0
F3-4	0	0	0	0	1	0	0	0	0	0	**2**	**0**	0	0	0	0
F3-6	0	0	0	1	1	0	0	33	67	25	**0**	**0**	0	0	0	0
F3-7	0	0	0	0	1	0	0	0	0	0	**2**	**0**	0	50	0	0
F3-9	3	0	0	1	1	0	0	0	0	0	**0**	**0**	0	0	0	0
F4-1	3	0	0	2	2	0	0	0	0	0	**2**	**0**	0	0	0	0
F5-1	5	19	10	7	5	0	0	0	0	0	**0**	**0**	25	0	0	0
F5-2	5	6	1	1	1	0	0	0	0	0	**2**	**0**	0	0	0	0
F5-5	8	6	14	14	8	0	0	0	0	0	**0**	**0**	0	0	0	0
F5-8	8	0	0	4	2	0	0	0	0	0	**0**	**0**	0	0	20	29
F5-9	3	3	0	4	2	0	0	0	0	0	**0**	**0**	0	0	0	0
F5-12	10	0	13	12	6	0	0	0	0	0	**0**	**0**	0	0	0	0
F5-36	8	0	1	2	2	0	0	0	0	0	**0**	**0**	0	0	0	0
Deletion	0	0	0	0	0	0	0	0	0	0	**0**	**0**	25	0	0	0
Other	8	13	6	4	5	0	0	0	0	0	**2**	**0**	0	0	0	0
No valid reaction	**10**	**16**	**7**	**11**	**10**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**

4.6 Vaccination prospects N. meningitidis

In the Netherlands, vaccination against serogroup C meningococcal disease was introduced in June 2002. All children born on or after June 1st, 2001 were vaccinated at the age of 14 months as part of the regular National Immunisation Programme. In addition, between June 2002 and October 2002, children and adolescents from 12 months to 19 years were vaccinated. In 2016-2018, the number of cases of meningococcal W disease showed a dramatic increase in the Netherlands. In response, the MenC vaccine was replaced by a vaccine that protects against meningococcal sergroups A, C, W and Y as of 1 May 2018. Because meningococcal type W also affected older children and because carriage is highest in this age group, the vaccination has also been offered to teenagers in the year they turn 14, as of 1 October 2018, including a catch-up campaign for 14-18 year olds between October 2018-June 2019. In 2024, one case due to serogroup C and 4 cases due to serogroup W meningococcal disease were reported in patients < 25 years of age (Figure 4.8).

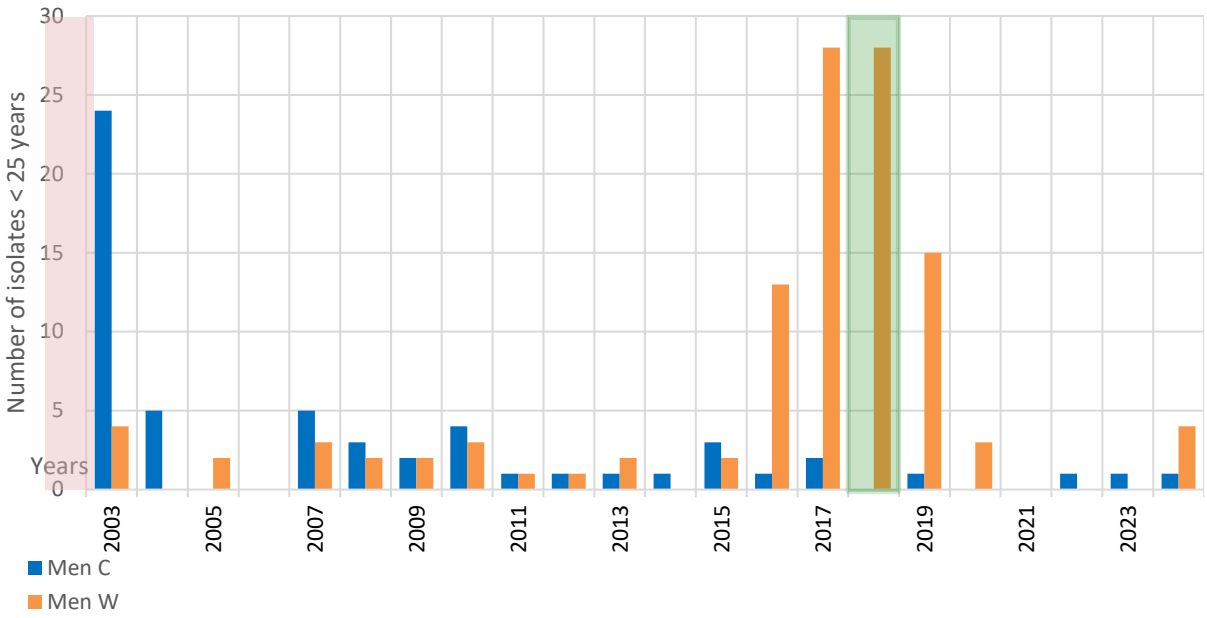


Figure 4.8 *Number of N.meningitidis serogroup C and W isolates in patients < 25 years of age, 2003-2024. Start of vaccination with MenC and MenACWY vaccine is indicated in orange and green color, respectively.*

Two meningococcal group B vaccines are registered in the Netherlands but not included in the National Immunisation programme (RIVM, meningococcal B vaccination).[6] [7]

[6] RIVM. *Meningokokken B vaccinatie*. https://lci.rivm.nl/richtlijnen/meningokokken-b-vaccinatie

[7] RIVM. Meningococcal disease serogroup B. Updated information for the Dutch Health Council | RIVM

5 HAEMOPHILUS INFLUENZAE

5.1 General features

In total, 341 samples from patients with *Haemophilus influenzae*, 334 isolates from CSF and/or blood and 7 culture-negative/PCR-positive CSF or blood samples, were submitted to the NRLBM in 2024. This is an increase compared to the 314 isolates received in 2023 (table 2.3, figure 3.3, figure 5.1). Thirty-one isolates or samples were from CSF (or CSF and blood; 9%) and 310 from blood only (91%). Fifty-eight (17%) of the isolates/samples were *H. influenzae* type b (table 5.1).

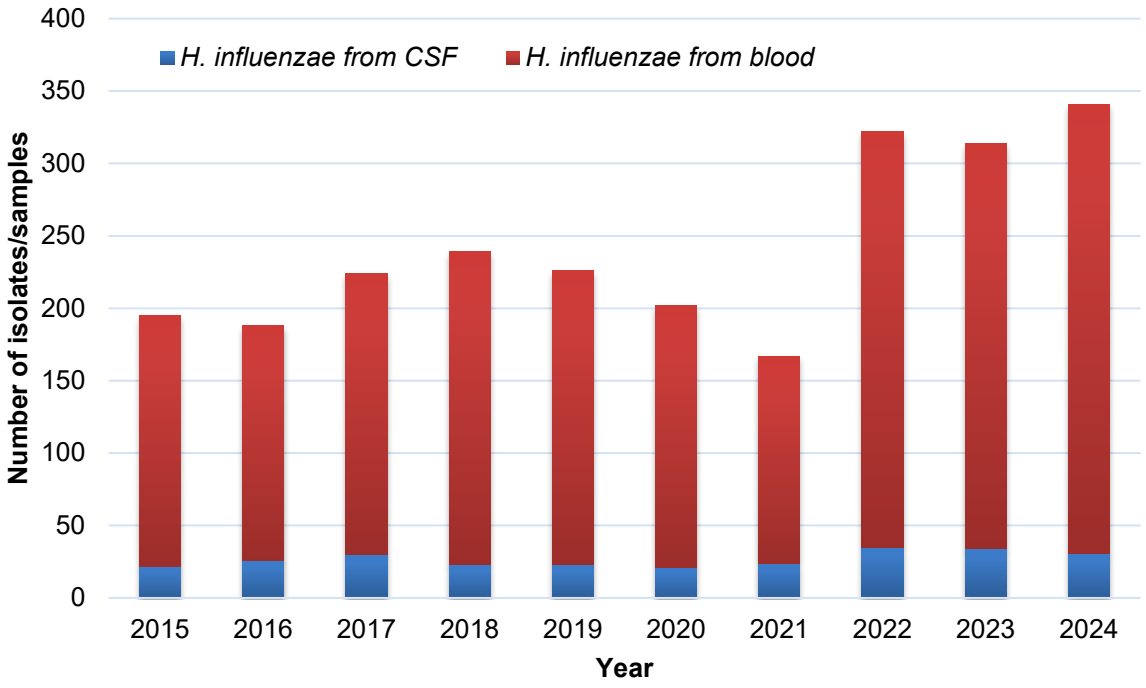


Figure 5.1 *Number of received H. influenzae isolates and CSF-positive samples according to isolation source, 2015-2024*

5.2 Antibiotic susceptibility

The proportion of ß-lactamase-producing invasive *H. influenzae* isolates (CSF and/or blood) was 10.6% in 2024 (Figure 5.2). Throughout the history of the NRLBM, the proportion of ß-lactamase-producing invasive *H. influenzae* isolates has always fluctuated for unknown reasons.

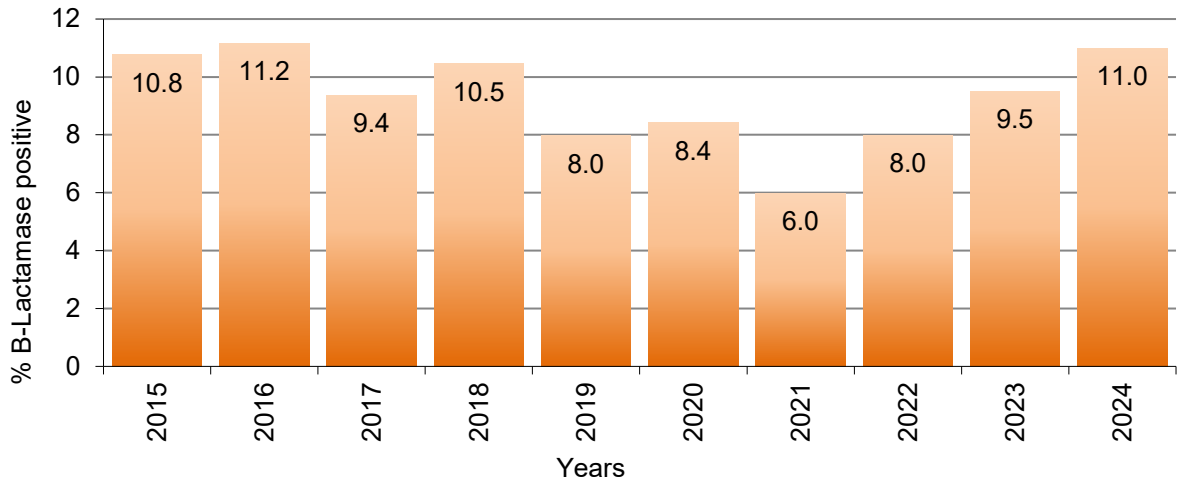


Figure 5.2 *Percentage β-lactamase-producing H. influenzae strains among received isolates, 2015-2024*

Between January – August, all CSF isolates and all typeable isolates (59) were assessed for penicillin susceptibility using the penicillin disc assay. From August onwards, antibiotic susceptibility testing (AST) was expanded to all *H. influenzae* isolates. In case the Pen-disc zone was <12 mm, AST to three additional antibiotics (ceftriaxon, augmentin, amoxicilline) was assessed using E-tests. All 46 isolates with a pen-disc zon <12 mm were sensitive to ceftriaxone, 44 (96%) of 46 were sensitive to augmentin of which 34 (77%) were also sensitive to amoxicillin. Two isolates were resistant to both augmentin and amoxicillin.

Penicillin- disc	β-lactamase Negative	β-lactamase Positive	TOTAL	
Not tested*	138	26	**164**	
Zone ≥ 12 mm; no b-lactam resistance	124	0	**124**	
Zone <12 mm	36	10	**46**	
Ceftriaxon – S (<0.19 mg/l)	*36*	*10*	***46***	
Augmentin – S (<3 mg/l)	*34*	*10*	***44***	
Augmentin– R (>2 mg/l)	*2*	*0*	***2***	
Amoxicilline – S (<3 mg/l)	*34*	*0*	***34***	
Amoxicilline – R (>2 mg/l)	*2*	*4*	***6***	
Amoxicilline – not tested	*0*	*6*	***6***	
Total	**298**	**36**	**334**	

*Not tested; Pen disc only tested for all CSF isolates and all other typeable isolates.

5.3 Serotype and age

In 2024, the number of *H. influenzae* type b isolates slightly increased to 58 compared to 52 isolates in 2023, representing 17% of all received *H. influenzae* isolates (17% in 2023, 19% in 2022, 41% in 2021, 30% in 2020 and 16% in 2019). Although this is proportionally returning back to pre-COVID-19 proportions. Since COVID-19, it is among the highest absolute number of Hib isolates since the introduction of the Hib vaccin (Figure 5.3). It is unclear what the underlying causes for these high number of Hib cases are.

We observed 15 cases (26%) of invasive Hib disease among children younger than 2 years of age (Table 5.1; 14 in 2023, 20 in 2022, 26 in 2021, 24 in 2020; 11 in 2019; 15 in 2018; 7 in 2017). The number of non-typeable *H. influenzae* isolates increased to 260, the highest number in the last 30 years (Figure 5.3 and table 5.2).Twenty-two (8.5%) non-typeable isolates were isolated from CSF (or CSF and blood) and 238 were isolated from blood only (table 5.1). Since 2000, the number of non-typeable *H. influenzae* isolates has steadily increased, which also explains the rise in total *H. influenzae* invasive infections over the same period (Figure 5.3). In addition, since 2008, the number of cases due to *H. influenzae* serotype f has been fluctuating but with an upward trend (Figure 5.3). Invasive disease with *H. influenzae* serotype f predominantly affects 50+ year olds (10 of 14, 71% in 2024; Table 5.1).

Table 5.1 Serotype distribution of all received *H. influenzae isolates* according to serotype patient's age, 2024

	AGE (MONTHS)				AGE (YEARS)					TOTAL	
Type	**0**	**1-11**	**12-23**	**24-59**	**0-4**	**5-9**	**10-19**	**20-49**	**≥50**	**T**	**%**
Hi - a	0	0	2	0	2	0	0	0	3	**5**	***1.5***
CSF	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	***0***	
Blood	*0*	*0*	*2*	*0*	*2*	*0*	*0*	*0*	*3*	***5***	
Hi - b	0	9	6	3	18	1	0	8	31	**58**	***17.0***
CSF	*0*	*3*	*1*	*2*	*6*	*1*	*0*	*0*	*1*	***8***	
Blood	*0*	*6*	*5*	*1*	*12*	*0*	*0*	*8*	*30*	***50***	
Hi - e	0	0	0	0	0	0	0	0	4	**4**	***1.2***
CSF	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	***0***	
Blood	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*4*	***4***	
Hi - f	0	1	0	0	1	0	0	3	10	**14**	**4.1**
CSF	*0*	*1*	*0*	*0*	*1*	*0*	*0*	*0*	*0*	***1***	
Blood	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*3*	*10*	***13***	
n.t.*	1	3	4	4	12	2	5	49	192	**260**	***76.2***
CSF	*0*	*1*	*2*	*1*	*4*	*1*	*0*	*3*	*14*	***22***	
Blood	*1*	*2*	*2*	*3*	*8*	*1*	*5*	*46*	*178*	***238***	
Total	**1**	**13**	**12**	**7**	**33**	**3**	**5**	**60**	**240**	**341**	***100.0***
CSF	***0***	***5***	***3***	***3***	***11***	***2***	***0***	***3***	***15***	***31***	***9.1***
Blood	***1***	***8***	***9***	***4***	***22***	***1***	***5***	***57***	***225***	***310***	***90.9***
%	***0.3***	***3.8***	***3.5***	***2.1***	***9.7***	***0.8***	***1.5***	***17.6***	***70.4***	***100.0***	

* non-typeable (and 2 CSF-PCR with high CP value, typing was not possible)

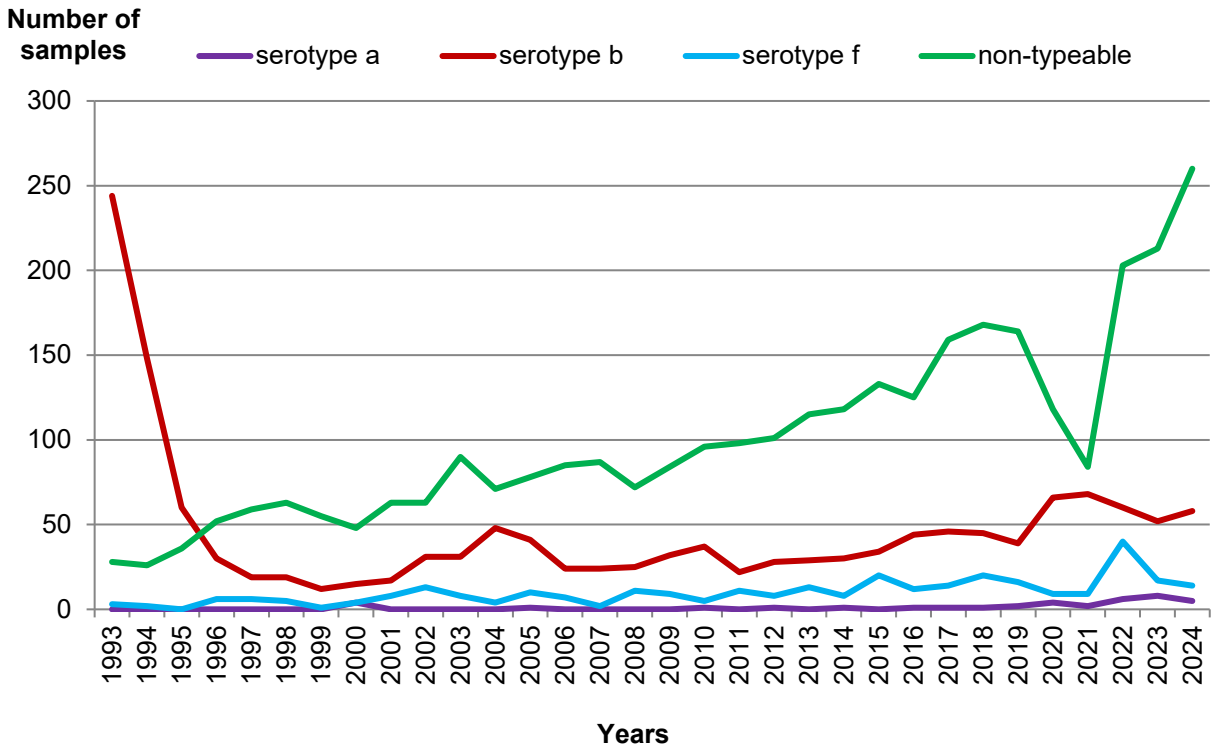


Figure 5.3 *Number of cases due to H. influenzae serotypes a, b, f and non-typeable H. influenzae, 1993-2024*

5.4 Distribution of non-typeable H. influenzae

The proportion of non-typeable *H. influenzae* isolates increased from 6% in 1992 to about 73% in 2019 (table 5.2). After a decrease to 50% in 2021 (table 5.2), non-typeable *H. influenzae* isolates again represented 76% of *H. influenzae* isolates in 2024. The vast majority of non-typeable *H. influenzae* isolates are from blood (92%) in accordance to previous years (Table 5.2). Seventy-three percent of invasive infections with non-typeable *H. influenzae* occurred in individuals of 50 years or older (Tables 5.1 and 5.2). Among non-typeable *H. influenzae* isolates, biotype II was the predominant biotype during the last ten years (Figure 5.5).

Table 5.2 Number and proportion of non-typeable *H.influenzae isolates* from CSF and/or blood according to age, 2015- 2024

n.t.	0-4	5-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	≥80	T	Csf / Blood	% **
2015	12	3	1	5	6	9	19	34	19	24	**132**	14/118	***67.7***
2016	10	1	0	3	6	6	9	39	25	24	**123**	10/113	***65.4***
2017	18	1	3	4	8	11	16	33	37	28	**159**	21/138	***71.0***
2018	16	2	7	5	8	9	14	30	32	45	**168**	9/159	***70.3***
2019	12	0	2	8	14	8	17	29	39	35	**164**	12/152	***72.6***
2020	9	2	4	5	2	7	13	24	30	21	**118**	5/113	***58.4***
2021	8	4	3	2	6	4	9	22	22	4	**84**	5/79	***50.3***
2022	20	2	2	10	23	3	24	45	36	44	**209**	19/190	***64.9***
2023	19	5	4	5	14	4	15	43	56	62	**232**	19/213	***73.9***
2024	12	2	5	16	20	13	16	50	64	61	**260***	22/238	***76.2***

* One patient without date of birth

** % non-typeable / total *H. influenzae* isolates

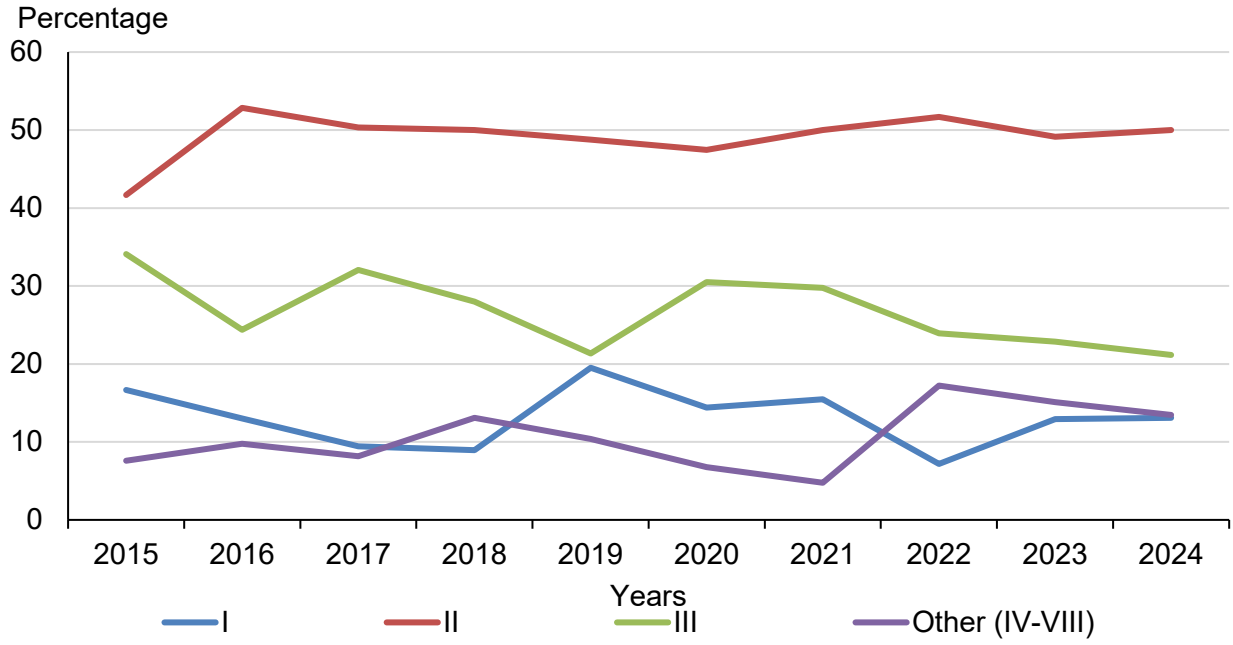


Figure 5.5 *Biotype distributions of non-typeable H. influenzae isolates from CSF and/or blood from 2015 – 2024.*

5.5 Geographical distribution of H. influenza

We plotted the geographical distribution of all *H. influenzae* cases (Fig. 5.7A) and *H. influenzae* b cases (Fig. 5.7B) per 100,000 inhabitants based on the patient's residence to identify whether there was indication for clustering. No apparent pattern emerged from this visualization.

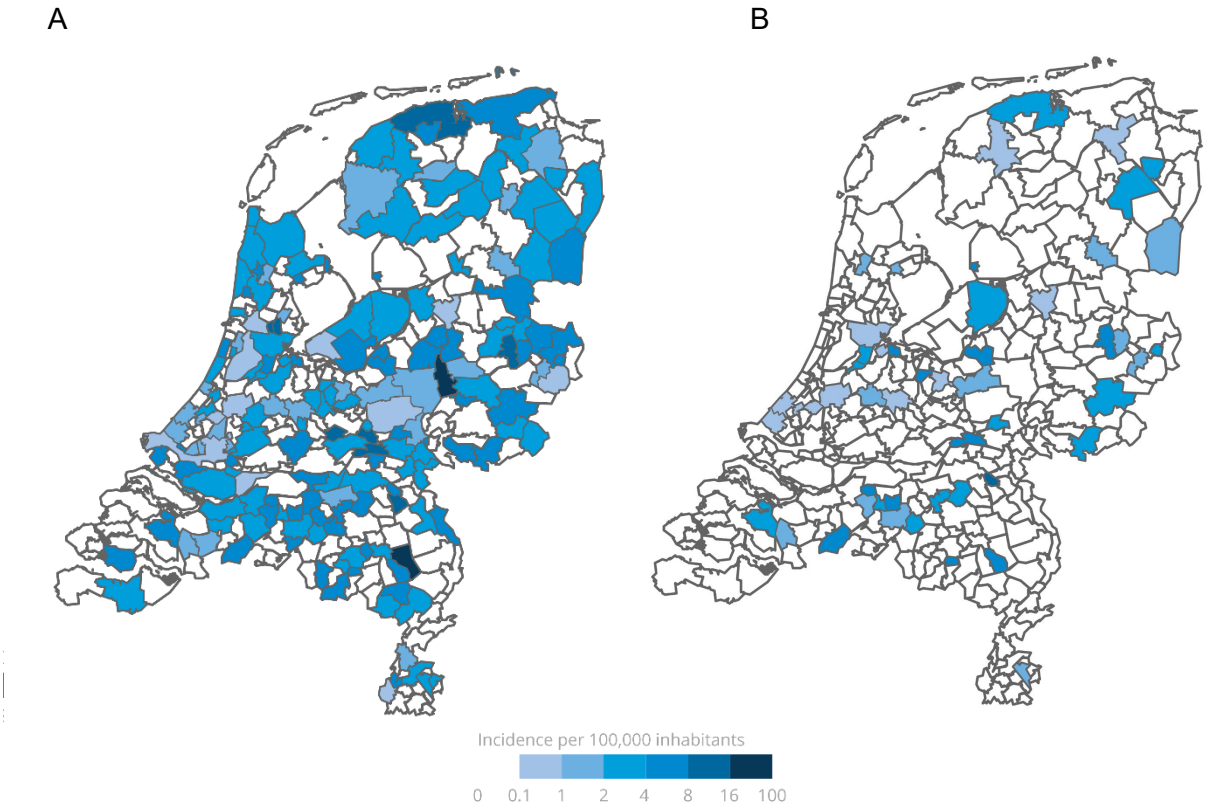


Figure 5.6. Geographical visualization of H. influenzae incidence for (A) all *H. influenzae* types and (B) *H. influenzae* b cases. Incidence is calculated per 100,000 inhabitants and place of residence of patient.

5.6 Vaccination prospects H. influenzae

The first implemented *H. influenzae* b vaccine consisted of the type b capsular polysaccharide conjugated to the tetanus toxoid protein (PRP-T). Since July 1993, children born after the 1st of April 1993 were vaccinated with the PRP-T vaccine, at the ages of 3, 4, 5, and 11 months. In 1999, the vaccine was administrated at the age of 2, 3, 4 and 11 months. In 2002, the Hib vaccine was given in combination with a pentavalent combination consisting of DTwP-IPV/Hib, with the whole cell pertussis (wP) component being changed to the acellular pertussis vaccine in 2004 (DTaP-IPV/Hib). In 2011, the Hepatitis B vaccine was added to this pentavalent combination vaccine (DTP3a-HBV-IPV/Hib). From Dec 2018, a different hexavalent vaccine product was used in which the composition of the administrated Hib conjugate vaccine changed from a conjugate with tetanus toxoid to a conjugate with *N. meningitidis* outer membrane protein complex (DTP5a-HBV-IPV-Hib). Finally, the standard vaccination schedule for this hexavalent vaccine that includes the Hib component has changed from a 3+1 to a 2+1 schedule (administrated at 3, 5, and 11 months of age) from January 2020.

The effect of vaccination on the frequency of *H. influenzae* meningitis cases is shown in figure 5.8. The number of *H. influenzae* meningitis cases caused by *H. influenzae* type b showed a steep decline since the introduction of the vaccine, while the number of cases caused by *H. influenzae* non-type b remained similar. In 2024, we received 20 *H. influenzae* type b isolates from patients that were vaccine-eligible (<31 years of age); 7 patients were CSF culture positive (CSF cases 2023: 12; 2022: 34; 2021: 11; 2020: 9) and 13 from blood (figures 5.8 and 5.9). Of the 20 patients, 9 were completely vaccinated, 9 patients were not (completely) vaccinated and from two patients, vaccination status was unknown.

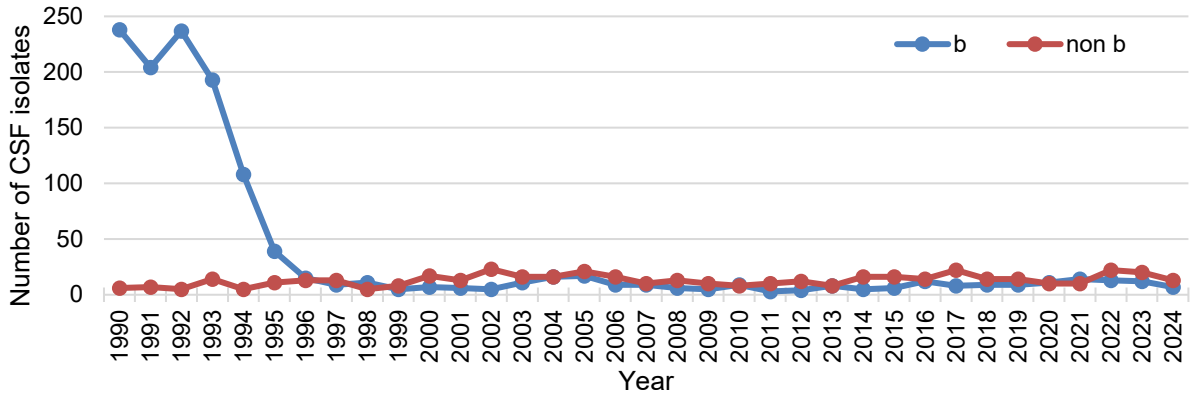


Figure 5.8 *The number of H. influenzae type b and non-type b cases from CSF, 1990 – 2024*

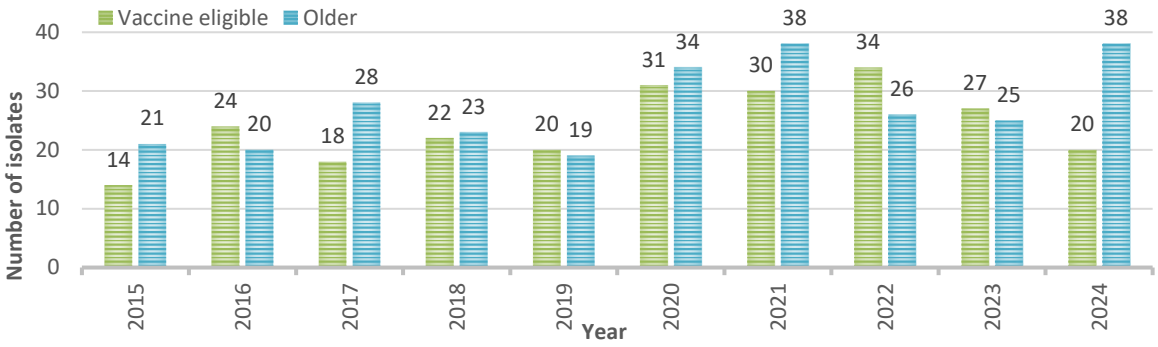


Figure 5.9 *The number of H. influenzae type b cases (CSF or blood) among patients eligible for vaccination and among non-vaccine eligible (older) patients, 2015 –2024*

6 STREPTOCOCCUS PNEUMONIAE

6.1 General features

From 2003 - 2023, the NRLBM requested nine sentinel laboratories (covering 25% of the Dutch population, 2020-2024; 28%), evenly distributed across the country, to submit pneumococcal isolates from blood from patients of all ages. In addition, all medical microbiology laboratories (MMLs) were requested to submit pneumococcal isolates from CSF (or CSF and blood), with confirmed or suspected meningitis from patient of all ages. From 2006, the 7-valent pneumococcal polysaccharide conjugate vaccine (PCV7) was introduced in the National Immunisation Programme and all MMLs were requested to submit pneumococcal isolates from patients with invasive disease in the age group 0-4 years. PCV7 was replaced by the 10-valent pneumococcal polysaccharide conjugate vaccine (PCV10) from March 1, 2011. .. Criteria for isolate submission remained similar until 2017. From 2017 onwards, all MMLs were requested to submit all invasive pneumococcal isolates without restriction to age of the patient. Due to the changes in the microbiology diagnostics landscape, with merging MMLs, it became challenging to reliably estimate the coverage of the original sentinel lab infrastructure. Therefore, from 2024 onward, data as obtained from all MMLs are reported. To allow comparison with previous years, the data from previous years will be extrapolated to the national level through multiplication with the correct coverage factor.

In 2024, the NRLBM received 2,187 isolates (or PCR-positive samples). Of the 2,187 nationwide submitted isolates, 143 (6.5%) isolates and 13 (0.6%) PCR-positive, culture negative sample were from CSF (or CSF and blood). The incidence of pneumococcal meningitis gradually increased from 1.0 per 100,000 individuals in 1990 to 1.6 per 100,000 individuals in 2004. The introduction of the PCV7/PCV10/PCV23 vaccin decreased pneumococcal meningitis incidence to 0.9 per 100,000 individuals in 2024 (Figure 6.1).

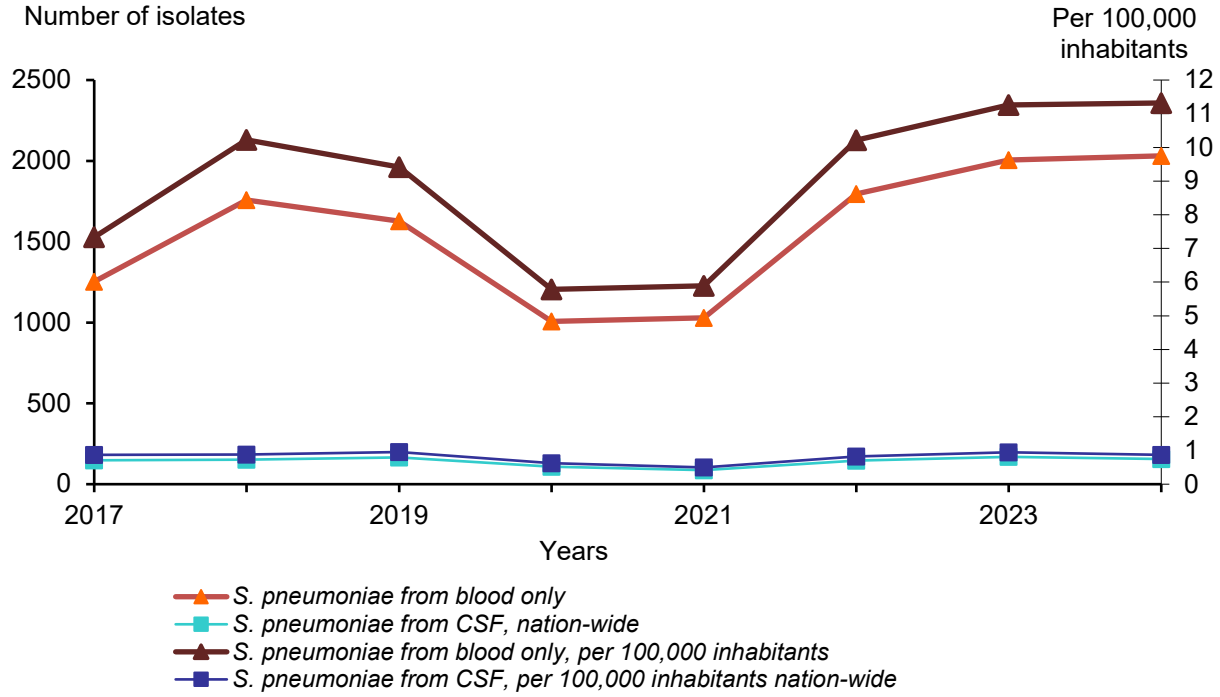


Figure 6.1 *Number of submitted S. pneumoniae isolates or PCR-positive samples from blood or CSF and invasive pneumococcal disease incidence based , 2017-2024*

Figure 6.2 shows the number of *S. pneumoniae* isolates/samples and incidence according to the patients' age group. The incidence of pneumococcal meningitis (CSF or CSF/blood) is highest among patients in the age groups 0-4, 60-64 and 70-74 years (Figure 6.2; top graph), whereas the incidence of pneumococcal bacteremia increases strongly from 60 years of age and is highest in 90-94 years olds (Figure 6.2; bottom graph). The absolute number of isolates from patients with bacteremia is highest in the age group 60-79 years (Figure 6.2; bottom graph). Figure 6.3 shows the geographical distribution of invasive pneumococcal disease per township based on patient's place of residence and per 100,000 inhabitants. There is no apparent pattern of clustering of cases.

.

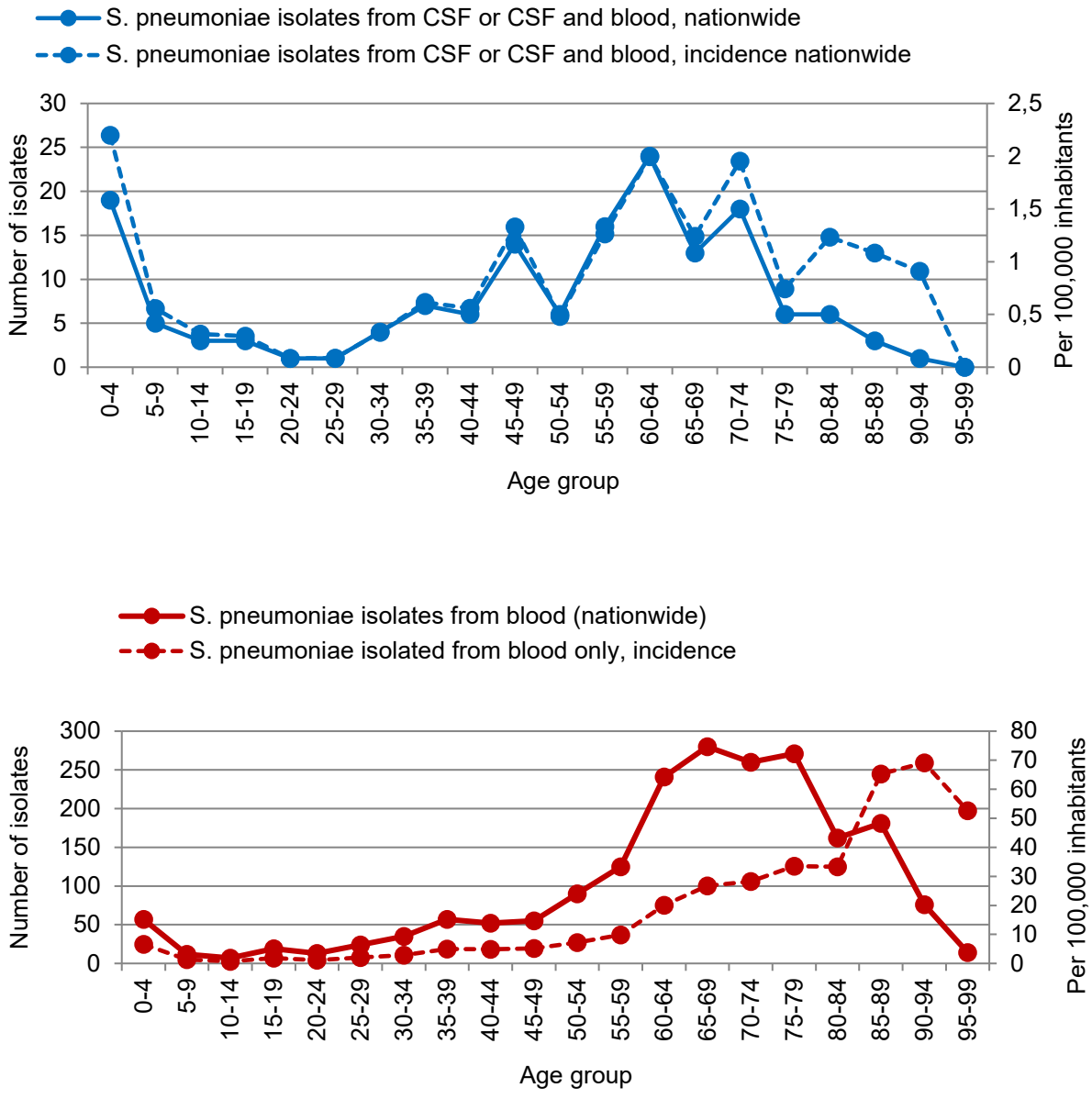


Figure 6.2 *S. pneumoniae isolates received per age group and incidence per 100,000 inhabitants according to isolation source in 2024. Top graph: isolates from CSF/CSF and blood. Bottom graph: isolates from blood only, nationwide*

S. pneumonia meningitis

S. pneumonia bacteremia

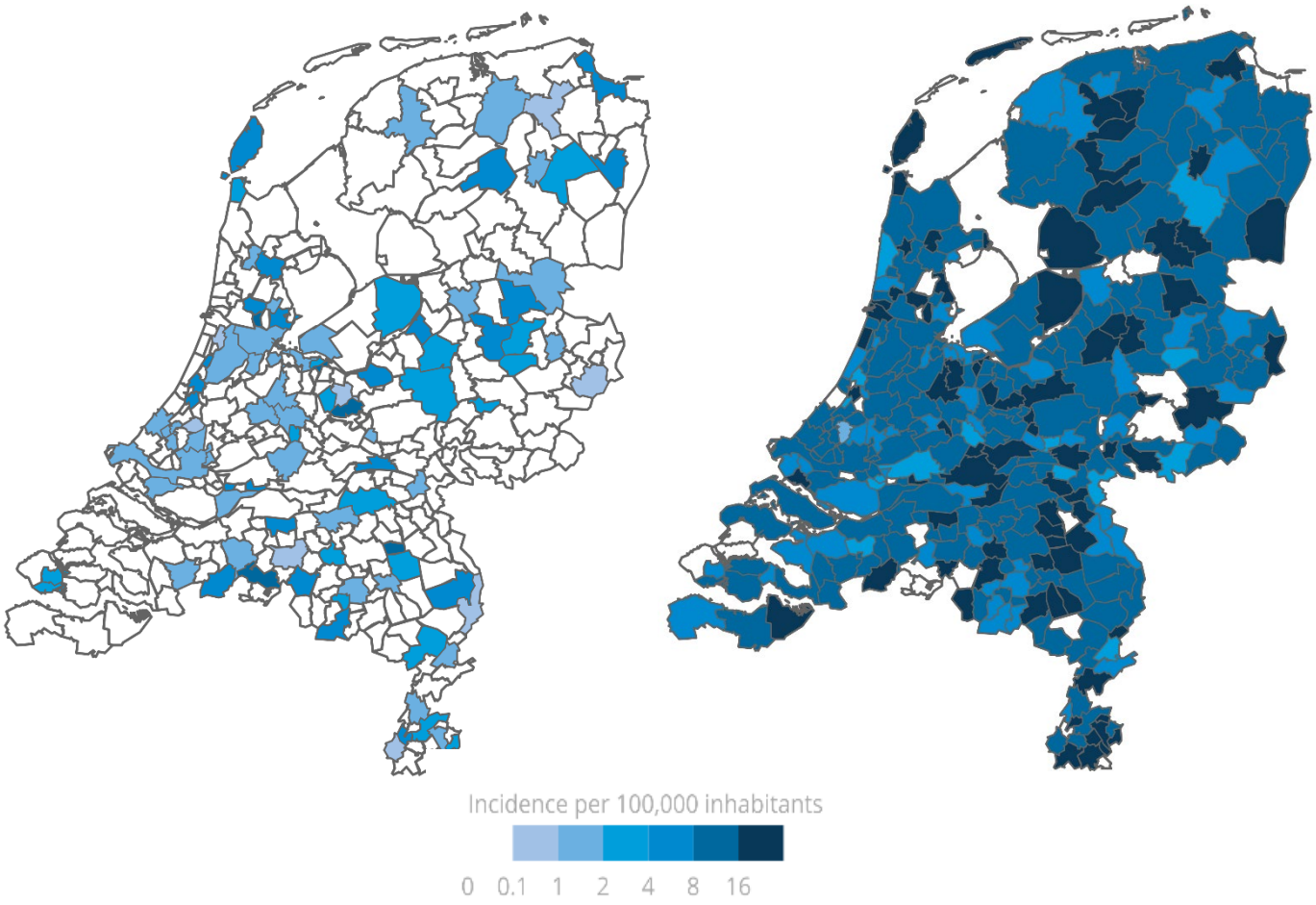


Figure 6.3 *Geographical distribution of S. pneumoniae invasive disease incidence per 100,000 inhabitants, left; patients with meningitis based on isolates/samples from CSF or CSF and blood, right; patients with bacteremia based on isolates from blood only (nationwide). Data plotted based on patient's place of residence (2024).*

6.2 Antibiotic susceptibility

Among 2,187 isolates, 143 (6.5%) were from CSF and 2,031 from blood only. Of the blood isolates, 182 (9%) were intermediately susceptible (0.06 < MIC ≤ 2.0 mg/L) and nine (0.4%) were resistant to penicillin (Table 6.1). Of the CSF isolates, 16 (10%) were resistant to penicillin (Table 6.1). From 13 patients (nationwide), no MIC values were obtained as no *S. pneumoniae* isolate was available (culture negative – PCR positive).

Table 6.1 Penicillin* susceptibility of *S. pneumoniae* isolates, 2024

MIC for CSF isolates (Nationwide)	S MIC ≤ 0.06	I 0.06< MIC ≤ 2.0	R MIC > 0.06	ND** (PCR)	Total
CSF/CSF and blood	127 (81.4%)	n.a.	16 (10.3%)	13 (8.3%)	156
Blood only	1840 (90.6%)	182 (9.0%)	9 (0.4%)	0	2031

* MIC values in mg/L according to EUCAST guidelines
** No MIC value known because no isolate was available (PCR-positive culture-negative sample)
n.a. not applicable for meningitis

6.3 Distribution according to serotype

The distribution of serotypes, grouped by vaccine type (VT) and by age of the patient, for isolates from CSF (or CSF and blood, nationwide) or blood only is presented in tables 6.2 and 6.4, respectively. Disease caused by PCV10-covered serotypes was 5.8% for meningitis (table 6.2) and 6.8% for bacteremia (table 6.4). Serotypes that would be additionally covered by the PCV13 vaccine (serotypes 3, 6A and 19A) accounted for approximately 28.8% and 28.6% of all isolates from meningitis and bacteremia patients, respectively (Tables 6.2, 6.4). Serotypes that would be covered by the PCV15 vaccine (all types covered by PCV13 plus 22F and 33F) account for approximately 42.9% and 44.9% of all isolates from meningitis and bacteremia patients, respectively (Tables 6.2, 6.4). The incidence of pneumococcal meningitis per 100,000 inhabitants per vaccine type and age of the patient is shown in table 6.3. Incidence of meningitis caused by PCV10 vaccine types is nearly eliminated in all age groups. Nonetheless, meningitis incidence is still highest in the age group 0-11 months, followed by non-vaccinated age groups, especially 50-79 years of age, as a result of disease caused by non-PCV10 serotypes (Table 6.3). For bacteremia, the incidence per 100,000 persons is shown in Table 6.5. Incidence is highest in the 80+ year olds and the 23-valent serotypes. For the children, incidence is the highest in the 0-11 month old, which is in the same range as for the 50-64 year olds. With the replacement of PCV10 for PCV15 in the National Immunization program, it is expected that the pneumococcal bacteremia incidence caused by PCV15 serotypes will significantly decrease in the coming years.

Effect of vaccin introduction on serotype distribution among meningitis and bacteremia is visualizedtables 6.5 and 6.6, respectively. The overall reduction in the number of PCV10-covered serotypes for the period 2011-2024 for meningitis isolates is 90%. However, the overall number of invasive pneumococcal disease isolates has remained fairly consistent up to 2019 due to an increase in the number of isolates of non-vaccine serotypes. Especially serotypes 3, 8 and 19A have been increasing over these years. Serotypes 3 and 19A together cause approximately 27% and 28% of all meningitis and bacteremia cases, respectively, and would be covered by PCV13. Of the non-PCV13 serotypes, serotype 8 is most prevalent in meningitis (9.0%; Table 6.2) and invasive pneumococcal disease in blood (15.5%; Table 6.4), which is included in PPV23 and the new conjugate vaccine PCV20.

Table 6.2 Serotype and age distribution of *S. pneumoniae* isolates from CSF (or CSF and blood; nationwide isolation collection), 2024. Serotypes are grouped by vaccine type.

				AGE (MONTHS)			AGE (YEARS)											
			TYPE	0	1-11	12-59	0-4	5-9	10-14	15-19	20-29	30-39	40-49	50-64	65-79	≥80	Total	%
23-valent vaccine	15-valent vaccine	13-valent vaccine	10-valent vaccine	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				4	-	-	-	-	-	-	-	-	-	1	2	2	-	5	**3.2**
				5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				6B	-	-	-	-	1	-	-	-	-	-	-	-	1	2	**1.3**
				7F	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				9V	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				14	-	-	-	-	-	-	-	-	-	-	-	-	1	1	**0.6**
				18C	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				19F	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				23F	-	-	-	-	-	-	-	-	-	-	1	-	-	1	**0.6**
				Subtotal	-	-	-	-	*1*	-	-	-	-	*1*	*3*	*2*	*2*	*9*	***5.8***
				3	-	-	1	1	2	-	-	2	2	6	10	4	1	28	**17.9**
				6A	-	-	-	-	-	-	-	-	-	-	-	2	1	3	**1.9**
				19A	1	4	-	5	-	-	-	-	2	1	2	3	1	14	**9.0**
				Subtotal	1	4	1	6	3	-	-	2	4	8	15	11	5	54	***34.6***
				22F	-	-	-	-	-	-	-	-	-	-	5	2	-	7	**4.5**
				33F	-	2	-	2	-	-	-	-	1	-	1	1	1	6	**3.8**
				Subtotal	1	6	1	8	3	-	-	2	5	8	21	14	6	67	***42.9***
				2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				8	-	-	-	-	-	-	-	-	-	4	6	4	-	14	**9.0**
				9N	-	1	-	1	-	1	-	-	-	1	1	3	-	7	**4.5**
				10A	-	-	1	1	-	-	-	-	-	1	4	2	3	11	**7.1**
				11A	-	-	-	-	-	-	-	-	1	-	1	-	-	2	**1.3**
				12F	-	-	-	-	-	-	-	-	1	1	3	1	-	6	**3.8**
				15B	-	1	-	1	-	1	-	-	-	-	1	-	-	3	**1.9**
				17F	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				20	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				Subtotal	*1*	*8*	*2*	*11*	*3*	*2*	-	*2*	*7*	*15*	*37*	*24*	*9*	*110*	***70.5***
				Other	-	3	2	5	-	-	2	-	1	5	9	10	1	33	***21.2***
				NT*	-	1	2	3	2	1	1	-	3	-	-	3	-	13	***8.3***
				Total	**1**	**12**	**6**	**19**	**5**	**3**	**3**	**2**	**11**	**20**	**46**	**37**	**10**	**156**	***100.0***

*Total 23 valent vaccine= sum of all above types – 6A
* From 3 patients with a pneumococcus detected in CSF there is no serotype known

Table 6.3 Age-specific incidence of pneumococcal meningitis nationwide (isolates from CSF or CSF and blood) per 100,000 inhabitants according to vaccine serotype, 2024

TYPE	0	1-4	5-9	10-14	15-19	20-29	30-39	40-49	50-64	65-79	≥80	Total
10-valent	-	-	0.11	-	-	-	-	0.05	0.08	0.07	0.22	0.05
13-valent	3.04	0.14	0.33	-	-	0.08	0.17	0.38	0.40	0.40	0.56	0.30
15-valent	4.26	0.14	0.33	-	-	0.08	0.21	0.38	0.57	0.50	0.67	0.37
23-valent	5.47	0.29	0.33	0.21	0.10	0.08	0.30	0.71	1.00	0.86	1.00	0.61
Other	1.82	0.29	-	-	0.20	-	0.04	0.24	0.24	0.36	0.11	0.18
Unknown	0.61	0.29	0.22	0.11	0.10	-	0.13	-	-	0.11	-	0.07
Total	**7.90**	**0.86**	**0.56**	**0.32**	**0.29**	**0.08**	**0.47**	**0.94**	**1.24**	**1.33**	**1.11**	**0.87**

Table 6.4 Serotype and age-dependent distribution of *S. pneumoniae* isolates from blood submitted nation wide, 2024.

				TYPE	AGE (MONTHS) 0	1-11	12-59	AGE (YEARS) 0-4	5-9	10-14	15-19	20-29	30-39	40-49	50-64	65-79	≥80	Total	%
23-valent vaccine	15-valent vaccine	13-valent vaccine	10-valent vaccine	1	-	-	-	-	-	-	-	-	-	-	-	1	-	1	***0.05***
				4	-	-	-	-	-	-	1	3	8	12	26	14	5	69	***3.4***
				5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	***-***
				6B	-	-	-	-	-	-	-	-	-	-	1	-	1	2	***0.1***
				7F	-	-	-	-	-	-	-	-	-	1	-	2	-	3	***0.15***
				9V	-	-	-	-	-	-	-	-	-	-	-	-	1	1	***0.05***
				14	-	-	1	1	2	-	1	3	5	6	6	22	8	54	***2.7***
				18C	-	-	-	-	-	-	-	-	-	-	-	-	-	-	***-***
				19F	-	-	-	-	-	-	-	-	-	1	2	2	1	6	***0.3***
				23F	-	-	-	-	-	-	-	-	-	-	1	-	1	2	***0.1***
				Subtotal	*-*	*-*	*1*	*1*	*2*	*-*	*2*	*6*	*13*	*20*	*36*	*41*	*17*	*138*	***6.8***
				3	-	1	1	2	1	-	-	2	6	11	44	101	53	220	***10.8***
				6A	-	-	-	-	1	-	-	-	-	-	-	2	1	4	***0.2***
				19A	1	7	12	20	3	-	1	8	22	10	82	136	76	358	***17.6***
				Subtotal	*1*	*8*	*14*	*23*	*7*	*-*	*3*	*16*	*41*	*41*	*162*	*280*	*147*	*720*	***35.4***
				22F	1	1	2	4	-	1	1	1	3	4	33	59	30	136	***6.7***
				33F	-	1	2	3	-	-	1	1	3	-	9	29	10	56	***2.7***
				Subtotal	*2*	*10*	*18*	*30*	*7*	*1*	*5*	*18*	*47*	*45*	*58*	*116*	*187*	*912*	***44.9***
				2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	***-***
				8	-	1	-	1	3	1	5	10	20	27	91	104	52	314	***15.5***
				9N	-	-	2	2	1	-	-	1	6	7	32	52	43	144	***7.1***
				10A	-	3	2	5	-	2	-	-		1	11	17	13	49	***2.4***
				11A	1	-	1	2	-	-	-	-	1	2	8	17	8	38	***1.9***
				12F	-	1	1	2	-	2	-	3	6	11	24	36	10	94	***4.6***
				15B	-	1	-	1	-	-	1	-		1	3	7	7	20	***1.0***
				17F	-	-	-	-	-	-	-	-	2	1	3	7	9	22	***1.1***
				20	-	-	-	-	-	-	-	-		2	5	6	7	20	***1.0***
				Subtotal	*3*	*16*	*24*	*43*	*11*	*6*	*11*	*32*	*82*	*97*	*381*	*614*	*336*	*1613*	***79.4***
				Other	-	3	11	14	1	1	8	5	10	10	75	197	97	418	***20.6***
				Total	**3**	**19**	**35**	**57**	**12**	**7**	**19**	**37**	**92**	**107**	**456**	**811**	**433**	**2031**	***100.0***

*Total 23 valent vaccine= sum of all above types – 6A

Table 6.5 Age-specific incidence of pneumococcal isolates from blood, nationwide per 100,000 inhabitants according to vaccine serotype, 2024

TYPE	0	1-4	5-9	10-14	15-19	20-29	30-39	40-49	50-64	65-79	≥80	Total
10-valent	-	0.14	0.22	-	0.20	0.25	0.56	0.94	0.97	1.48	1.89	0.77
13-valent	5.47	2.00	0.78	-	0.29	0.68	1.75	1.93	4.37	10.08	16.32	4.01
15-valent	7.30	2.57	0.78	0.11	0.49	0.76	2.01	2.12	1.56	4.18	20.76	5.08
23-valent	11.55	3.43	1.22	0.63	1.08	1.36	3.50	4.56	10.27	22.11	37.31	8.99
Other	1.82	1.57	0.11	0.11	0.78	0.21	0.43	0.47	2.02	7.10	10.77	2.33
Total	**13.38**	**5.00**	**1.34**	**0.74**	**1.86**	**1.57**	**3.93**	**5.04**	**12.29**	**29.21**	**48.07**	**11.32**

Table 6.6 Changes in serotype distribution of pneumococcal CSF isolates (nationwide isolate collection). Introduction of PCV10 in Immunisation Programme in 2011 is shaded in gray, 2014-2024

		TYPE	2011	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
23-valent vaccine (all above types except 6A)	15-valent vaccine	13-valent vaccine	10-valent vaccine	1	1	4	1	2	1	-	-	-	-	-	-	-
				4	2	2	-	1	1	2	1	-	1	5	4	5
				5	-	-	-	-	-	-	-	-	-	-	-	-
				6B	2	-	1	-	-	-	-	2	-	-	-	2
				7F	28	8	7	4	2	2	1	-	-	-	-	-
				9V	-	1	-	2	-	-	-	-	-	-	-	-
				14	2	-	1	-	-	2	-	-	-	1	2	1
				18C	5	-	1	-	1	1	1	-	-	-	-	-
				19F	6	4	2	5	6	1	3	1	1	5	3	-
				23F	2	-	1	-	1	-	-	-	-	1	-	1
				Subtotal PCV10	*48*	*19*	*14*	*14*	*12*	*8*	*6*	*3*	*2*	*12*	*9*	*9*
				3	7	13	16	25	20	20	21	20	16	15	22	28
				6A (not in PPV23)	1	3	-	1	-	-	-	-	-	-	1	3
				19A	16	7	10	8	16	13	20	15	7	18	21	14
				Subtotal PCV13	*72*	*42*	*40*	*48*	*48*	*41*	*47*	*38*	*25*	*45*	*53*	*54*
				22F	16	8	11	11	8	8	10	6	3	7	8	7
				33F	5	2	4	4	6	6	3	1	3	5	8	6
				Subtotal PCV15	93	52	55	63	62	55	60	45	31	57	69	67
				2	-	-	-	-	-	-	-	-	-	-	-	-
				8	17	23	24	18	21	23	26	8	14	20	20	14
				9N	7	6	6	3	6	4	4	4	4	2	7	7
				10A	7	12	5	7	7	7	11	2	3	11	9	11
				11A	5	3	2	3	2	8	-	4	-	1	3	2
				12F	7	8	9	12	8	11	5	3	-	2	3	6
				15B	3	-	-	5	7	2	7	1	2	3	1	-
				17F	3	1	-	-	1	2	-	1	2	2	3	3
				20	-	1	1	-	-	-	-	-	-	1	-	-
				Subtotal PPV23*	*141*	*103*	*102*	*110*	*114*	*112*	*113*	*68*	*56*	*99*	*114*	*107*
				6C	4	3	6	5	3	3	11	12	3	6	4	5
				7B	-	-	-	-	-	-	-	2	-	-	-	-
				7C	-	-	-	-	-	-	1	-	1	2	-	1
				10F	-	-	-	-	-	-	-	-	-	-	-	-
				10B	-	1	1	-	1	-	1	1	1	1	3	-
				11D	-	-	-	-	-	-	-	-	-	1	-	-
				12A	-	-	-	-	-	-	-	-	-	-	-	-
				13	-	-	-	-	-	-	-	-	1	-	-	-
				15F	1	6	7	2	4	3	1	-	2	-	3	1
				15A	-	-	-	-	-	-	-	-	-	1	-	-
				15C	-	-	1	-	3	1	1	1	1	1	2	2
				16F	4	2	1	3	1	5	-	-	1	1	2	1
				17A	-	-	-	-	-	-	-	-	-	-	-	-
				18F	-	-	-	-	-	-	-	-	-	-	-	-
				18A or B	-	-	-	-	-	-	-	-	-	-	-	-
				21	1	-	-	-	-	2	-	1	1	1	-	-
				22A	-	-	1	1	-	-	-	-	-	-	-	-
				23A	2	4	5	5	5	8	6	5	1	3	6	7
				23B	2	8	11	6	11	8	10	9	10	12	11	8
				24F	1	7	7	1	2	1	5	-	-	1	-	4
				24B	-	-	-	-	-	-	-	-	-	-	-	-
				27	-	2	1	1	-	1	1	1	-	2	3	-
				28A	1	-	-	-	-	-	-	-	-	-	-	-
				29	-	-	-	-	-	-	-	-	-	-	-	1
				31	-	1	-	1	1	-	-	-	-	-	-	-
				33A	-	-	-	-	-	-	-	-	-	-	-	-
				34	1	-	1	1	1	2	2	1	-	1	1	1
				35F	1	1	2	5	1	3	3	4	2	6	4	1
				35A	-	-	-	-	-	-	-	-	-	-	1	-
				35B	-	1	1	1	-	2	-	-	-	1	1	-
				35D	-	-	-	-	-	1	1	-	-	-	-	-
				37	1	-	-	-	-	-	-	-	-	-	-	-
				38	-	-	-	-	-	-	2	-	-	-	-	1
				Rough (n.t.)/ Unknown	-	-	-	-	1	-	10	3	7	7	13	13
				Subtotal Non vaccin	21	36	45	32	34	40	52	40	31	46	54	46
				Total	163	142	147	143	148	152	165	108	87	145	169	156

Table 6.7 Changes in serotype distribution of pneumococcal blood isolates (nationwide isolate collection). Introduction of PCV10 vaccin in 2011 is shaded in gray, 2017-2024

			TYPE	2011*	* x4	2017	2018	2019	2020	2021	2022	2023	2024
23-valent vaccine (all above types except 6A)	15-valent vaccine	13-valent vaccine	10-valent vaccine	1	40	160	20	15	5	-	-	-	-	1
				4	27	108	9	15	7	18	14	33	54	69
				5	11	44	1	-	-	-	-	-	-	-
				6B	3	1*	3	6	4	3	2	3	4	2
				7F	91	364	43	50	19	7	2	3	3	3
				9V	5	20	3	5	2	1	1	2	1	1
				14	19	76	15	21	32	13	7	17	19	54
				18C	8	32	2	4	2	2	1	2	1	-
				19F	9	36	14	15	7	9	3	10	11	6
				23F	5	20	3	5	3	2	3	4	5	2
			Subtotal PCV10		218	872	113	136	81	55	33	74	98	138
				3	36	144	106	166	124	94	99	233	268	220
				6A (not in PPV23)	2	8	6	10	5	3	5	6	2	4
				19A	63	252	173	260	257	162	224	383	363	358
			Subtotal PCV13		319	1,276	398	572	467	314	361	696	731	720
				22F	37	148	76	106	105	60	49	126	191	136
				33F	15	60	31	66	45	27	24	41	65	56
			Subtotal PCV15		371	1,484	505	744	617	401	434	863	987	912
				2	-	-	1	-	-	-	-	-	-	-
				8	59	236	312	455	454	253	230	355	316	314
				9N	17	68	69	95	87	53	41	53	72	144
				10A	14	56	25	31	27	29	21	36	42	49
				11A	9	36	19	32	32	18	23	19	31	38
				12F	19	76	62	54	80	32	15	49	77	94
				15B	4	16	18	19	21	11	14	18	17	20
				17F	8	32	13	12	11	9	16	20	13	22
				20	4	16	8	10	20	4	6	20	22	20
			Subtotal PPV23*		505	2,012	1,032	1,452	1,349	810	800	1,433	1,577	1,613
				6C	7	28	35	66	56	52	55	72	102	91
				6D	-	-	-	-	-	-	-	-	2	2
				7B	-	-	1	2	3	5	1	4	1	3
				7C	-	-	-	2	15	20	9	24	31	27
				7D	-	-	-	-	-	-	-	-	1	-
				10F	-	-	-	1	-	-	-	-	-	-
				10B	-	-	2	6	6	3	4	4	6	5
				11B	-	-	-	-	2	-	-	-	2	-
				11D	-	-	-	1	7	3	3	2	1	-
				12A	-	-	-	1	-	-	-	-	-	-
				13	1	4	1	-	-	-	-	-	2	1
				15F	-	-	-	-	-	-	1	-	-	-
				15A	2	8	38	44	21	23	27	46	37	41
				15C	2	8	6	7	6	4	6	9	18	10
				16F	7	28	18	14	15	11	16	27	24	28
				17A	2	8	-	-	-	-	-	-	-	-
				18F	-	-	-	-	1	-	-	-	1	-
				18A or B	1	4	-	-	2	-	-	-	3	-
				21	-	-	2	3	-	4	2	1	1	3
				22A	1	4	-	3	-	-	-	-	-	-
				23A	2	8	25	38	32	18	30	45	55	43
				23B	9	36	30	40	48	13	37	43	47	62
				24F	3	12	16	16	18	9	3	22	16	28
				24A	-	-	1	-	-	-	-	-	-	2
				24B	-	-	-	-	-	-	1	1	-	-
				25F	-	-	1	-	-	-	-	-	-	-
				25A	-	-	-	-	-	-	-	-	1	-
				27	1	4	-	2	4	1	1	1	-	2
				28A	-	-	1	-	1	-	-	1	-	-
				29	-	-	1	1	1	-	-	1	-	-
				31	2	8	7	9	6	1	2	8	3	11
				33A	-	-	-	1	-	-	-	-	-	-
				34	-	-	3	6	7	3	3	4	8	5
				35F	6	24	15	14	9	14	12	22	16	20
				35A	-	-	-	2	-	-	-	-	-	1

	35B	3	*12*	6	18	10	7	10	11	13	10
	35C	-	-	-	-	-	1	-	-	-	-
	35D	-	-	-	-	2	-	3	2	2	-
	37	-	-	1	-	-	-	1	1	1	2
	38	3	*12*	9	6	4	5	1	7	33	20
	48	-	-	-	-	1	-	-	-	-	-
	Rough (n.t.)/ unknown	2	*8*	2	2	2	-	2	5	2	1
	Subtotal Non Vaccin	54	*216*	221	305	279	197	230	363	429	418
	Total	559	*2236*	1253	1757	1628	1007	1030	1796	2006	2031

6.4 Vaccination

The first pneumococcal polysaccharide conjugated vaccine contained 7 serotype-specific polysaccharides linked to inactive diphtheria toxin (PCV7). Since July 2006, children born after the 1st April 2006 were vaccinated with PCV7 with a 3+1 schedule at the ages of 2, 3, 4 and 11 months. In April 2011, the 10-valent vaccine (PCV10) was introduced for all newborns from March 1st 2011. Since autumn 2024, PVC10 is replaced with PCV15 for all newborns from November 2023; initially only for the booster vaccination and from approximately January 2025 onwards, for all 3 doses. In 2024, 5.8% of the CSF isolates were of a serotype covered by the PCV10 vaccine (table 6.2). There were 9 patients with pneumococcal meningitis due to pneumococci with a PCV10 vaccine serotype (4, 6B, 14 and 23F; Table 6.6). Only one patient was born after April 2006 and was therefore eligible for PCV10 vaccination. The beneficial effect of vaccination is partly countered by an increase in the number of cases due to non-vaccine types (Figure 6.4).

The pneumococcal polysaccharide vaccine covers 23 serotypes (PPV23). Seventy-one percent of the CSF isolates and 79.4% of blood isolates were of a serotype that would be covered by this vaccine (Table 6.6 and Table 6.7). (2005: 90% pre-vaccination). From 2020, PPV23 was offered through the National Immunisation Programme to the elderly in yearly cohorts (2020: 1941-1947, 2021: 1948-1953, 2022:1953-1956, 2023: 1956-1961, 2024: 1961-1964), covering the ages 60-83 years. From autumn 2025 onwards, PPV23 is replaced with PCV20.

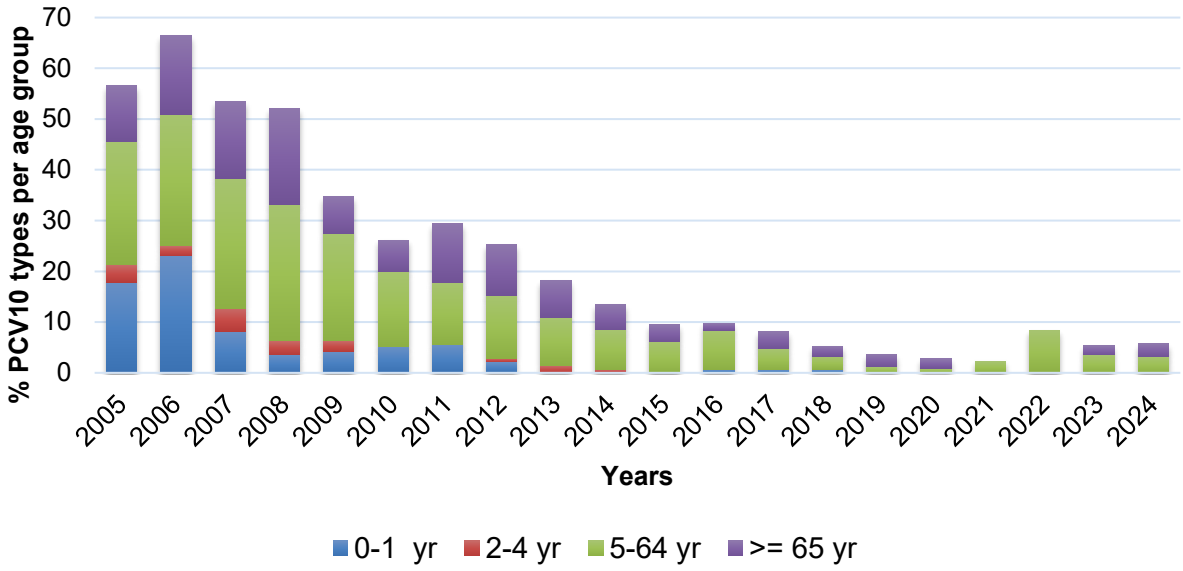


Figure 6.4 *Proportion of PCV10 serotypes in patients with invasive pneumococcal disease per age category, 2005-2024.*

7 ESCHERICHIA COLI

The NRLBM received 109 *Escherichia coli* isolates, 11 isolated from CSF (or CSF and blood) and 98 from blood only (Figure 7.1, Table 7.1). Nearly all isolates (106; 97%) were from children < 1 year of age, whereas 3 isolates (all CSF) were from patients older than 47 years. Sixty-six percent (n=72) of the *E. coli* meningitis and bacteremia cases occurred in the first month of life (Table 7.1). Before 2016, the number of received isolates was rather stable with 15-30 isolates per year. From 2017, there has been a marked increase, especially in received blood isolates, which is at least partly explained by increased submission as result of an ongoing study on neonatal meningitis (NOGBS study)[8]. Since 2019, isolate submission has stabilized around 95 isolates per year (Figure 7.1), with a slight increase in 2024.

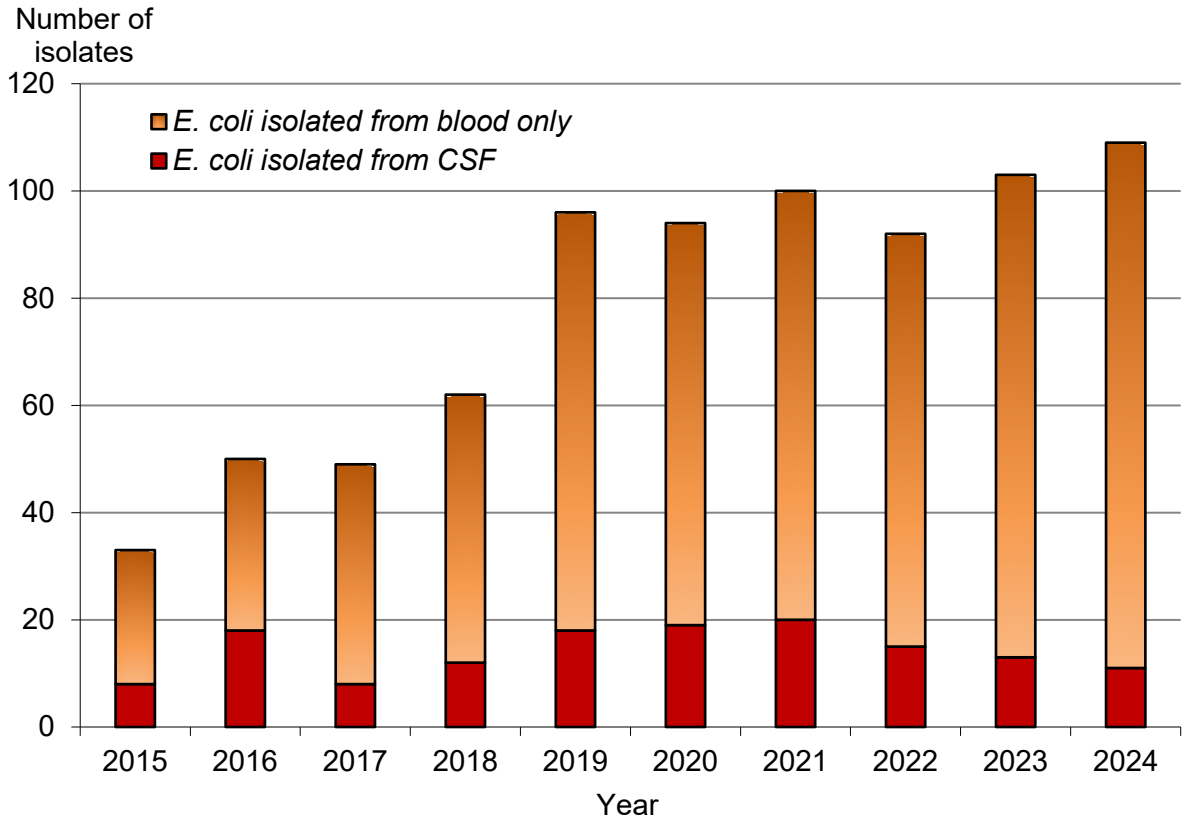


Figure 7.1 *Number of E. coli isolates received according to isolation source, 2015-2024*

Since 2016, K1 expression was determined by phage typing. Since January 2024, K1 presence was determined with Ouchterlony using cross-reactive Meningococcal group B antiserum. In 2024, approximately 44% of the received *E. coli* isolates carried the K1 antigen (Table 7.1). Of the 11 *E. coli* isolates from CSF (or CSF and blood) from children, 36% (n=4) expressed the K1 antigen. For blood isolates, the proportion of non-K1 expressing *E. coli* isolates was higher at 55% (54 from 98) compared to K1-expressing isolates (Table 7.1)

[8] *NOGBS study* Neuroinfecties Amsterdam: https://meningitisamc.nl/professionals/wetenschappelijk-onderzoek-professionals/nogbs-studie

Table 7.1 Number of *E. coli* isolates grouped according to serotype, patient's age, and source of isolation, i.e. CSF and/or blood, 2024

	AGE (MONTHS)			AGE (YEARS)					TOTAL	
Group	0	1-11	12-59	0-4	5-9	10-19	20-49	≥50	T	%
Non K1	39	19	0	58	0	0	1	2	**61**	***56***
CSF	*3*	*1*	*0*	*4*	*0*	*0*	*1*	*2*	***7***	
*Blood**	*36*	*18*	*0*	*54*	*0*	*0*	*0*	*0*	***54***	
K1	33	15	0	48	0	0	0	0	**48**	***44***
CSF	*2*	*2*	*0*	*4*	*0*	*0*	*0*	*0*	***4***	
Blood	*31*	*13*	*0*	*44*	*0*	*0*	*0*	*0*	***44***	
Total	**72**	**34**	**0**	**106**	*0*	*0*	*1*	*2*	**109**	***100***
CSF	*5*	*3*	*0*	*8*	*0*	*0*	*1*	*2*	*11*	*10*
Blood	*67*	*31*	*0*	98	*0*	*0*	*0*	*0*	*98*	*90*
%	***66***	***31***	***0***	***97***	***0***	***0***	***1***	***2***	***100***	

* Note: Submission criteria, all *E. coli* isolates from patients with meningitis. For invasive disease (meningitis and non-meningitis), *E. coli* isolates only from children < 1 year.

Since 2012, *E. coli* isolates received by the NRLBM are additionally characterized by O- and H-typing using Whole Genome Sequencing (through MicrobesNG, Birmingham, UK). O-typing refers to the genes within the O-antigen gene clusters, whereas H-typing determines the H-antigen genes that encode for the different flagellar types. Among the K1 isolates, 28% were of H-type H7 and 21% of type H4. H-type H4 was also dominant among the non-K1 isolates (31%), with H1 and H5 accounting together for almost sixty-fivex percent of the non-K1 isolates (table 7.2).

Table 7.2 H-type distribution among K1 and non-K1 *E. coli* isolates from CSF or blood, 2020-2024

TYPE	K1 / Non K1	K1 / Non K1	K1 / Non K1	K1 / Non K1	K1 / Non K1
	2020	**2021**	**2022**	**2023**	**2024**
H1	0 / 5	0 / 9	0 / 11	0 / 12	0 / 14
H4	8 / 8	11 / 12	8 / 9	6 / 13	10 / 19
H5	3 / 8	1 / 5	5 / 5	2 / 11	8 / 7
H6	6 / 0	4 / 2	2 / 2	5 / 2	11 / 4
H7	27 / 1	29 / 2	26 / 3	23 / 3	13 / 2
H9	0 / 1	0 / 2	-	0 / 1	-
H18	0 / 8	0 / 7	0 / 5	0 / 5	0 / 9
H31	0 / 4	5 / 1	3 / 4	3 / 1	2 / 3
Other	2 / 13	3 / 7	2 / 7	1 / 15	3 / 4
Total	**46 / 48**	**53 / 47**	**46 / 46**	**40 / 63**	**47/62**

The types O6 (23%) and O15 (15%) are most prevalent among non-K1 isolates, while the types O1 (19%) and O50/O2 (17%) are most frequent among K1 isolates. The isolates showed in the group 'Other' were all different O-types (Table 7.3).

Table 7.3 O-type distribution among K1 and non-K1 *E. coli* isolates from CSF or blood, 2020-2024

TYPE	K1 / Non K1	K1 / Non K1	K1 / Non K1	K1 / Non K1	K1 / Non K1
	2020	**2021**	**2022**	**2023**	**2024**
O1	15 / 1	14 / 1	15 / 3	9 / 11	9 / 0
O4	0 / 2	0 / 4	0 / 3	0 / 8	0 / 1
O6	0 / 7	0 / 6	1 / 11	1 / 4	0 / 14
O7	2 / 0	2 / 0	0 / 0	0 / 1	3 / 1
O15	0 / 5	0 / 6	0 / 3	1 / 5	2 / 9
O16	2 / 2	1 / 2	0 / 3	0 / 2	3 / 3
O18	6 / 1	11 / 0	2 / 0	9 / 2	3 / 1
O25	2 / 7	7 / 1	5 / 6	4 / 6	3 / 7
O45	1 / 0	2 / 0	5 / 0	0 / 0	0 / 0
O46	0 / 0	4 / 0	3 / 0	3 / 0	1 / 0
O50/O2	8 / 0	5 / 2	5 / 2	6 / 3	8 / 0
O75	3 / 2	1 / 1	3 / 0	2 / 5	6 / 4
O117/O107	0 / 2	0 / 3	4 / 1	0 / 3	1 / 7
Other	7 / 19	6 / 21	5 / 14	5 / 22	9 / 15
Total	**46 / 48**	**53 / 47**	**46 / 46**	**40 / 63**	**47/62**

Among K1 isolates, the O/H combination O1:H7 (17%) was most prevalent while among non-K1 isolates, O6:H1 (18%) was dominant (Figure 7.3).

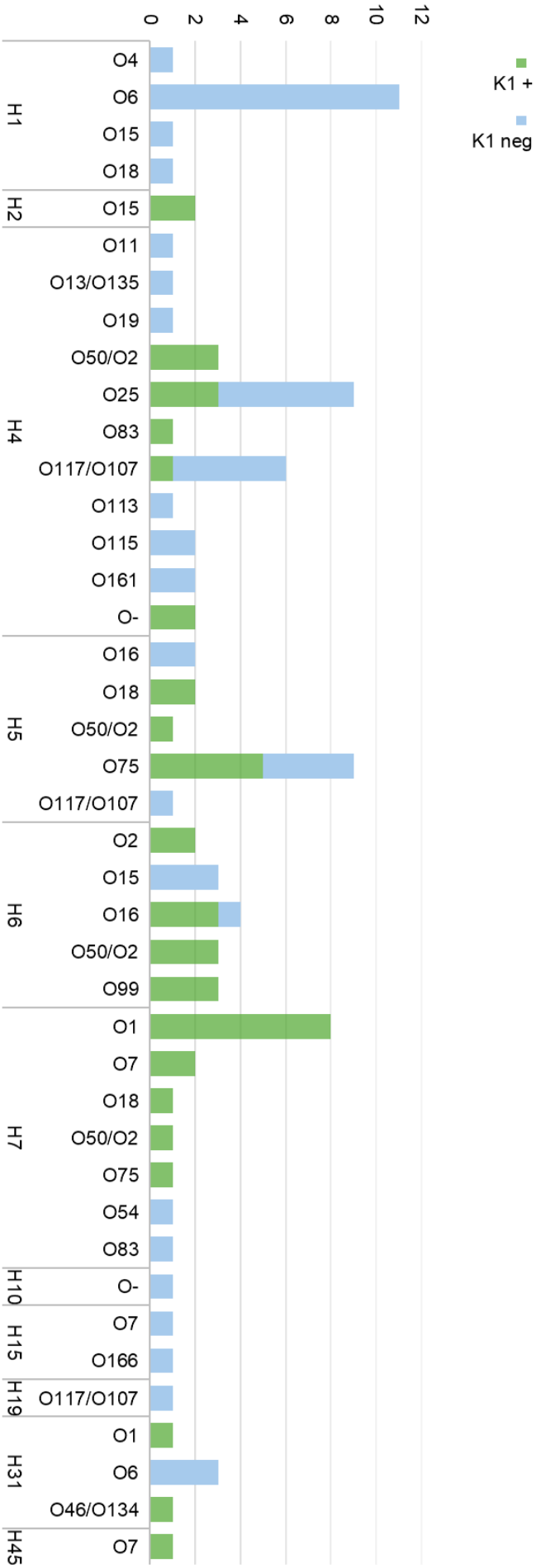


Figure 7.3 Distribution of H- and O-type combinations among K1 and non-K1 *E. coli* isolates from CSF and/or blood, 2024

8 STREPTOCOCCUS AGALACTIAE – (group B)

In 2024, the NRLBM received 86 *Streptococcus agalactiae* (Group B Streptococcus) isolates, which is a decrease compared to the 99 isolates in 2023, 116 isolates in 2022, 147 isolates in 2021 (figure 8.1). Nine (10%) *S. agalactiae* isolates were from CSF (or CSF and blood) and 77 (90%) from blood only (table 8.1, figure 8.1). Sixty-nine percent of all the cases (n=59) occurred in the first month of life, with 8% of the isolates recovered from CSF and 92% from blood (Table 8.1). As in previous years, Serotype III was most prevalent, accounting for 51% of the cases (table 8.1, figure 8.2), which is a decrease compared to previous years. In contrast, serotypes Ia and V increased in proportion from 15% to 21% and from 8% to 12%, respectively (Figure 8.2).

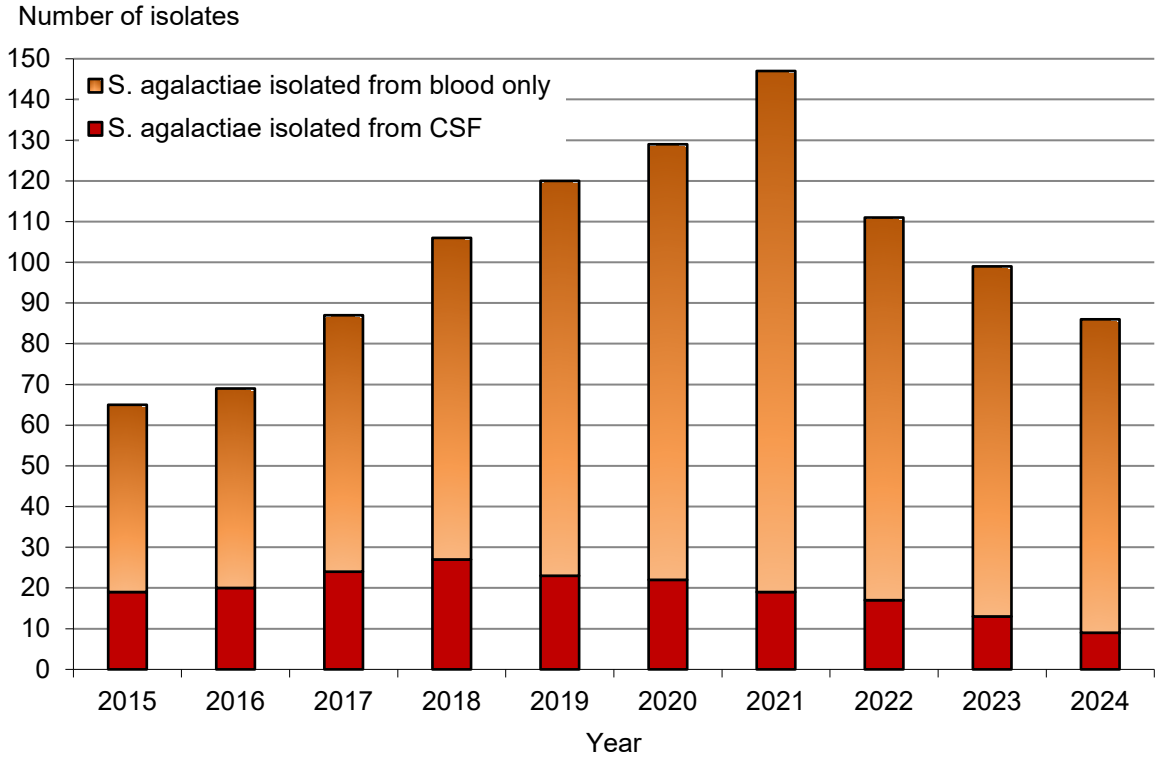


Figure 8.1 Number and source of *S. agalactiae isolates, 2015 - 2024*

Table 8.1 Serotype distribution of *S. agalactiae* isolates from CSF and/or blood by age of patients, 2024.

	AGE (MONTHS)			AGE (YEARS)					TOTAL	
Group*	**0**	**1-11**	**12-59**	**0-4**	**5-9**	**10-19**	**20-49**	**≥50**	**T**	**%**
Ia	11	6	0	17	0	0	0	1	**18**	***20.9***
CSF	*1*	-	-	*1*	-	-	-	-	***1***	
Blood	*10*	*6*	-	*16*	-	-	-	*1*	***17***	
Ib	0	2	0	2	0	0	0	1	**3**	***3.5***
CSF	-	*1*	-	*1*	-	-	-	*1*	***2***	
Blood	-	*1*	-	*1*	-	-	-	-	***1***	
II	2	0	0	2	0	0	1	0	**3**	***3.5***
CSF	-	-	-	-	-	-	-	-	***0***	
Blood	*2*	-	-	*2*	-	-	*1*	-	***3***	
III	35	9	0	44	0	0	0	0	**44**	***51.2***
CSF	*4*	-	-	*4*	-	-	-	-	***4***	
Blood	*31*	*9*	-	*40*	-	-	-	-	***40***	
IV	1	1	0	2	0	0	0	2	**4**	***4.7***
CSF	-	-	-	-	-	-	-	*1*	***1***	
Blood	*1*	*1*	-	*2*	-	-	-	*1*	***3***	
V	7	2	0	9	0	0	0	1	**10**	***11.6***
CSF	-	-	-	-	-	-	-	-	-	
Blood	*7*	*2*	-	*9*	-	-	-	*1*	***10***	
VI	1	0	0	1	0	0	0	0	**1**	***1.1***
CSF	-	-	-	-	-	-	-	-	-	
Blood	*1*	-	-	*1*	-	-	-	-	***1***	
IX	2	1	0	3	0	0	0	0	**3**	***3.5***
CSF	-	*1*	-	*1*	-	-	-	-	***1***	
Blood	*2*	-	-	*2*	-	-	-	-	***2***	
Total	**59**	**21**	**0**	**80**	**0**	**0**	**1**	**5**	**86**	***100***
CSF	***5***	***2***	***-***	***7***	***-***	***-***	***-***	***2***	***9***	***10.5***
Blood	***54***	***19***	***-***	***73***	***-***	***-***	***1***	***3***	***77***	***89.5***
%	***68.6***	***24.4***	***0***	***93.0***	***0***	***0***	***1.1***	***5.9***	***100.0***	

* Note: Submission criteria, all *S.agalactiae* isolates from patients with meningitis. For invasive disease (meninigitis and non meningitis), *S. agalactiae* isolates only from children < 1 year.

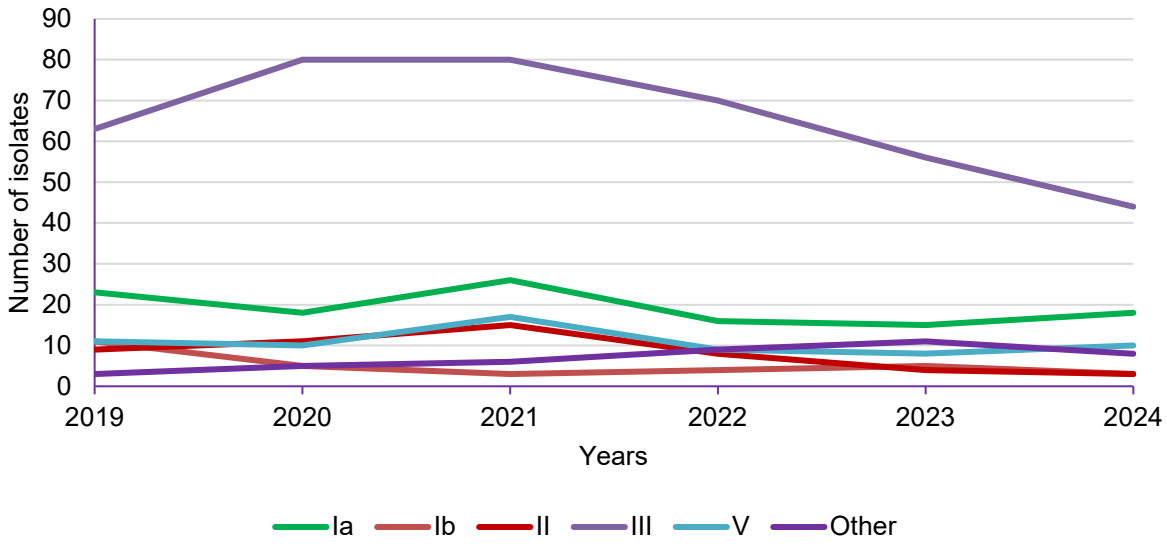


Figure 8.2 *Distribution of S. agalactiae serotypes, 2019 - 2024*

9 LISTERIA MONOCYTOGENES

In 2024, 113 *Listeria monocytogenes* isolates were submitted to the NRLBM, which is the highest number in the last 10 years (Figure 9.1). Of these, 20 (18%) were from CSF (or CSF and blood) and 93 (82%) from blood only (Figure 9.1, Table 9.1). The large majority (88%) of cases occurred among individuals over 50 years of age (Table 9.1). Similar to previous years, serotypes 1/2a and 4b were most prevalent in 2024 (Table 9.1), accounting for 24% and 61% of the cases, respectively. These proportions have been quite steady in the past five years except for 2022 (Figure 9.2).

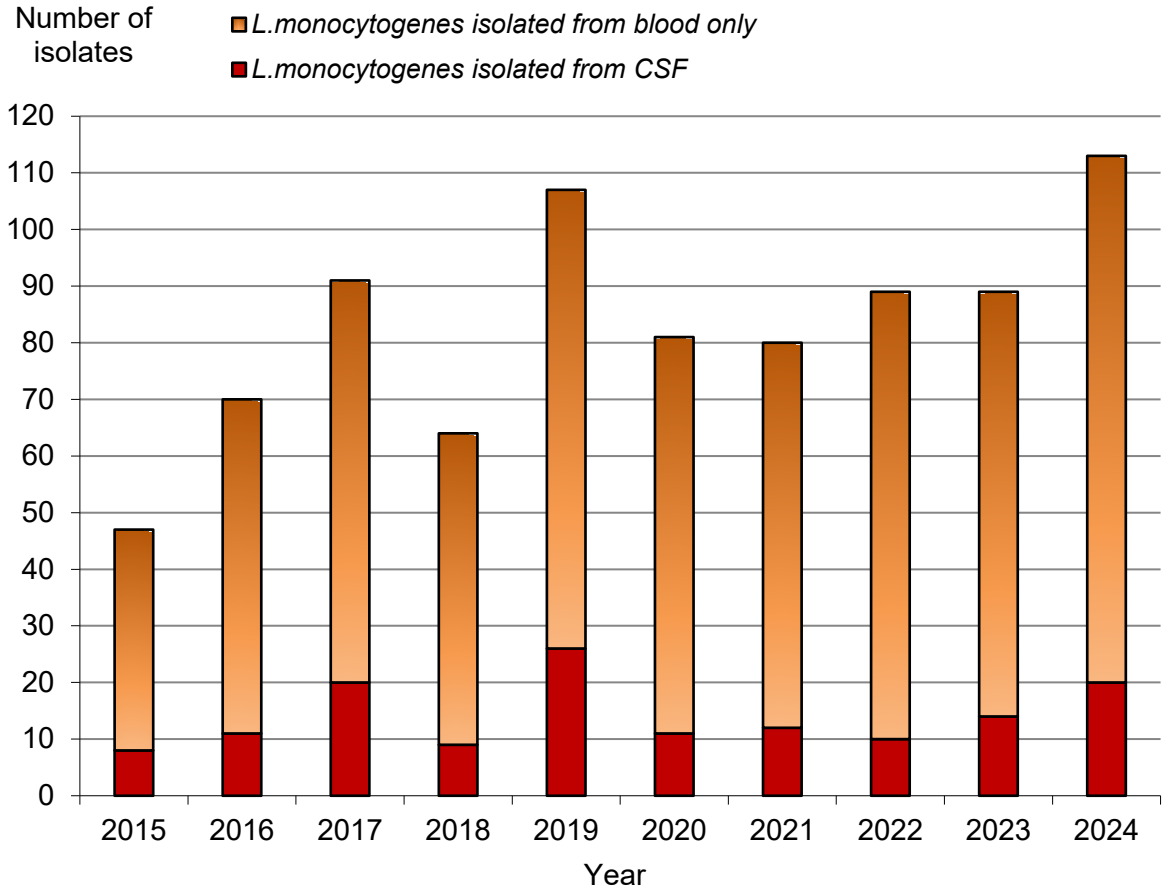


Figure 9.1 *Number of L. monocytogenes isolates grouped by isolation source, 2015-2024*

Table 9.1 Total number of *L. monocytogenes* isolates from CSF and/or blood grouped according to age of patient and serotype,

	AGE (YEARS)					TOTAL	
Group	**0-4**	**5-19**	**20-49**	**50-79**	**≥80**	**T**	**%**
1/2a	0	0	3	20	4	**27**	***23.9***
CSF	*0*	*0*	*0*	*4*	*0*	***4***	
Blood	*0*	*0*	*3*	*16*	*4*	***23***	
1/2b	0	0	2	8	3	**13**	***11.5***
CSF	*0*	*0*	*1*	*2*	*0*	***3***	
Blood	*0*	*0*	*1*	*6*	*3*	***10***	
1/2c	0	0	0	0	2	**2**	***1.8***
Blood	*0*	*0*	*0*	*0*	*2*	***2***	
4a	0	0	0	1	0	**1**	***0.9***
Blood	*0*	*0*	*0*	*1*	*0*	***1***	
4b	3	0	5	45	16	**69**	***61.0***
CSF	*2*	*0*	*1*	*9*	*0*	***12***	
Blood	*1*	*0*	*4*	*36*	*16*	***57***	
PCR pos	0	0	0	1	0	**1**	***0.9***
CSF	*0*	*0*	*0*	*1*	*0*	***1***	
Total	**3**	**0**	**10**	**75**	**25**	**113**	***100.0***
CSF	***2***	***0***	***2***	***16***	***0***	***20***	***17.7***
Blood	***1***	***0***	***8***	***59***	***25***	***93***	***82.3***
%	***2.7***	***0***	***8.8***	***66.4***	***22.1***	***100.0***	

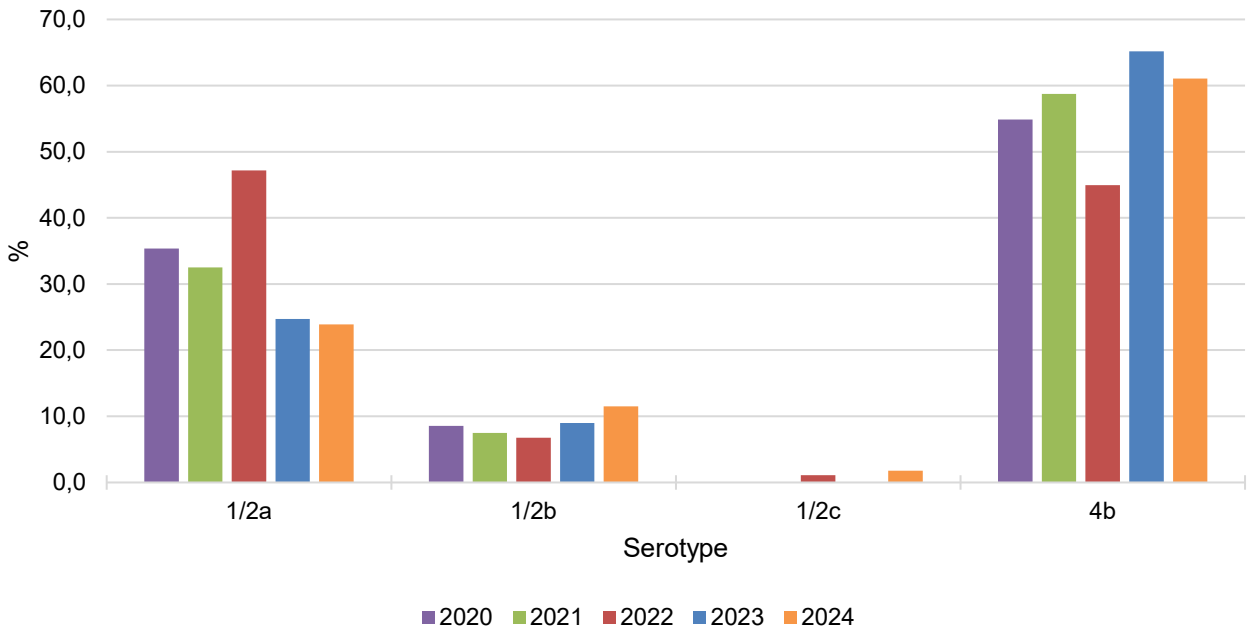


Figure 9.2 *Percentage of L. monocytogenes isolates grouped by serotype, 2020-2024*

10 STREPTOCOCCUS PYOGENES – (group A)

Until 2019, the NRLBM received *Streptococcus pyogenes* isolates associated with meningitis only. From April 2019, the NRLBM also received *S. pyogenes* isolates from other invasive infections (iGAS) that were submitted through 9 sentinel laboratories that cover approximately 28% of the Dutch population (same 9 sentinel laboratories as for *S. pneumoniae*). In addition, the NRLBM participated in a 2-year pilot study to gain insight into puerperal sepsis/fever caused by *S. pyogenes* at the national level (pGAS) starting in 2019 and ending July 2021. Finally, from April 2022, the NRLBM receives *S. pyogenes* isolates from all invasive infections (iGAS) from all MMLs and from January 2023 is considered to be active surveillance since all iGAS manifestations have become notifiable. We plan to publish the results from the complete iGAS surveillance in a separate report.

Since 2015, all received *S. pyogenes* isolates are *emm*-typed by sequencing the hypervariable part of the *emm* gene (CDC – Streptococcus Laboratory)[9], which encodes the surface-expressed M protein. Currently, over 220 different *emm* genotypes are recognized. In 2014, an *emm*-cluster based system was proposed, clustering related M proteins based on shared binding and functional properties (Sandersom-Smith, 2014)[10].

In 2024, 1347 *S. pyogenes* isolates from were submitted to the NRLBM, 13 were isolated from CSF and 10 were not isolated from CSF but with clinical suspicion for meningitis (Table 10.1). Over 60% of *S. pyogenes* meningitis cases occurred in adults above 20 years of age (Table 10.1).

Table 10.1 *S. pyogenes* isolates from CSF and/or non CSF with clinical suspicion for meningitis according to patient's age, 2024.

TYPE	AGE (YEARS)					TOTAL	
	0-4	**5-9**	**10-19**	**20-49**	**≥50**	**T**	%
CSF	0	2	3	5	3	**13**	***56.5***
Blood*	2	1	1	2	4	**10**	***43.5***
Total	**2**	**3**	**4**	**7**	**7**	**23**	***100***
%	***8.7***	***13.1***	***17.4***	***30.4***	***30.4***	***100***	

[9]CDC - Streptococcus Laboratory. Centers for Disease Control and Infections: https://www.cdc.gov/streplab/groupa-strep/resources.html

[10]Sanderson-Smith, M. D et al. A systematic and functional classification of *Streptococcus pyogenes* that serves as a new tool for molecular typing and vaccine development. *J Infect Dis* 2014.

The *emm* typing and *emm*-cluster based data of meningitis isolates are displayed in Table 10.2. There was a strong dominance of Cluster A-C5 (n=17; 74%), particularly caused by *emm3.93* (n=13; 57%) among *S. pyogenes* isolates from meningitis patients (Table 10.2).

Table 10.2 *Emm*-type and *emm*-cluster distribution of meningitis related *S. pyogenes* isolates, 2024

Cluster	emm type	CSF	Blood*	Total	%T
A-C3	1.0	0	1	1	***4.3***
A-C4	12.37	0	1	1	***4.3***
A-C5		10	7	17	***74.0***
	3.127	*0*	*1*	*1*	
	3.197	*1*	*0*	*1*	
	3.60	*0*	*2*	*2*	
	3.93	*9*	*4*	*13*	
Y	5.206	0	1	1	***4.3***
M6	6.4	2	0	2	***8.8***
No result		1	0	1	***4.3***
Total		**13***	**10**	**23**	***100***

*In one CSF sample only *S. pyogenes* DNA was detected. *Emm*-typing was not possible.

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