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Annual Report of the Swiss National Reference Center for Meningococci, 2025

Address

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Website: Italian: http://www.meningo.ch/index_IT.html

Website: English: http://www.meningo.ch/index_EN.html

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1. Introduction

Invasive meningococcal disease (IMD), caused by the bacterium *Neisseria meningitidis*, remains a persistant global health threat. *N. meningitidis* is a typical benign colonizer of the healty human nasopharynx. Colonized people spread the bacteria to others by respiratory secretions (e.g., by saliva droplets) [1, 2]. When the conditions are met in at risk-people, the transmitted bacteria invade the body and cause different types of illnesses, such as meningitis [3], sepsis [4], pneumonia [5], septic arthritis [6], pericarditis [7], or urethritis [8]. In many cases, IMD survivors suffer long-term sequelae. Developmental disorders, and hearing loss remain among the major neurological sequelae observed in the survivors of the disease [3]. Serogroups A, B, C, W and Y are the main serogroups of *N. meningitidis* responsible for IMD [3]. Over the past 25 years, the IMD epidemiology has undergone several geographical and temporal modifications based on patients' age and serogroups distribution. Thus, successful vaccination programs covering these five serogroups must be tailored to the local epidemiology. After an important decrease in incidence during the COVID-19 pandemic, the last 2-3 years have witnessed resurgences of IMD all over the globe, and primarily among unvaccinated risk groups [9]. The continued absence of IMD caused by rare serogroups (E, H, Z, I, K and L) and the predominance of serogroup B causing recent IMD outbreaks in Europe underline the need for large vaccination efforts against MenB besides that of serogroups ACWY [9, 10].

In 2024, 615 IMD cases were reported in France, the highest number of cases since 2010. In January 2025 alone, there were 90 IMD cases, and the identification of MenB clusters: students in Lyon in January 2025 and in Rennes between December 2024 and February 2025 with 6 cases caused by the same strain in two separate situations (a family and students) with no link between them. Cluster analysis revealed a MenB strain ST-485 (ST-41/44 clonal complex) / P1.12-1,16 :F1-5 : CC41/44 (ST-485).

The proportion of cases caused by MenB ST-485 has been gradually increasing in England since 2010. This strain has caused community-based outbreaks and clusters. ST-485 was the most common ST among MenB cases in England in 2022 [9]. Importantly, 3 IMD cases caused by MenB ST-485 were identified during February 2025 in the French Alps linked to the ski station Morzine *(source: Muhamed-Kheir Taha, Institut Pasteur, Invasive Bacterial Infections Unit, France)* but no MenB ST-485 cases were observed in Switzerland last year.

The immense majority of *N. meningitidis* strains involved in IMD are encapsulated. The capsule enables the resistance to the humoral immune response and its subsequent dissemination. In contrast, non-capsulated *N. meningitidis* strains are susceptible to opsonization and rarely implicated in invasive infections. However, a few cases of IMD caused by non-capsulated *N. meningitidis* were reported. A Japanese male taxi driver with an immunoglobulin G4 (IgG4)-related disease developed a bacteremia and meningitis caused by a non-capsulated strain [11]. In Switzerland, together with Dr Nina Lutz, we reported the first primary meningococcal arthritis caused by a non-encapsulated *N. meningitidis* strain in a previously healthy 52-year old man [12] .

The increasing antimicrobial resistance of important human pathogenic bacteria remains a key public health concern. Steady increase of multidrug-resistant *Neisseria gonorrhoeae* isolates represent one of the important threats worldwide [13]. In contrast, *N. meningitidis* seems relatively spared by the emergence of antibiotic resistance. Nevertheless, since the 1980s *N. meningitidis* isolates exhibiting decrease susceptibility to penicillin were reported in different countries [14, 15]. Nowadays, penicillin-resistant *N. meningitidis* strains are widely reported across the world [16]. The important mechanisms related to penicillin resistance are changes in five critical residues of PBP2 (F504L, A510V, I515V, H541N, and I566V) conferred by mutations in the *penA* gene [17]. Penicillin-resistant strains with high minimal inhibitory concentrations (MIC >2 mg/mL) were rarely described. High penicillin MIC are achieved by chromosomal or plasmid-mediated β-lactamase, the latter being derived from the *Haemophilus influenzae* ROB-1 β-lactamase (*bla* $_{ROB-1}$) [18]. *N. meningitidis* ST-3587, harbouring *bla* $_{ROB-1}$ and a mutated DNA gyrase (*gyrA*) has recently emerged in Europe [19]. In 2023, a MenY ST-3587 producing a *bla* $_{ROB-1}$ was identified in Switzerland for the first time.

N. meningitidis isolates with reduced susceptibility to third-generation cephalosporins (3GC) were reported during the last few years. This resistance profile was linked to the specific acquisition of an allele, *penA327*, which was mainly found in France but is beginning to spread throughout the world [20].

Neisseria isolates harbouring the *penA327* allele can mainly be found in the US, and 93% of these isolates are *N. gonorrhoeae*. Since 2012, *penA327* has been identified in *N. meningitidis*, suggesting horizontal gene transfer from gonococci to meningococci during co-infection/co-colonization through sexual transmission of both bacteria [20].

In Switzerland, invasive meningococcal diseases have to be reported to the Swiss Federal Office of Public Health (SFOPH), and corresponding isolates should be referred to the Swiss National Reference Center for Meningococci (CNM, Centre National des Méningocoques; http://www.meningo.ch) at the University Hospital in Geneva.

The CNM provides reference testing of invasive *N. meningitidis* isolates in collaboration with the SFOPH, and currently performs serotyping and molecular typing following protocols recommended by the European Meningococcal Disease Society (EMGM) (http://emgm.eu). Based on a combination of serogroup and molecular typing data, each strain is classified and data are integrated into national (SFOPH) and international epidemiological databases (European Meningococcal Epidemiology in Real Time [EMERT] database; http://emgm.eu/emert) in order to monitor and share information about trends in distribution of meningococcal populations. This methodology is evolving towards Next Generation Sequencing (NGS) [21], a method that we used for a selection of cases collected between 2010 and 2016, to determine the clonality of the meningococcal strains of serogroup W finetype (PorA 5,2:FetA 1-1:ST-11). This was executed as a separate subproject supported by the SFOPH (Decision 16.928412). This annual report describes the methods used and the results obtained at the CNM during the calendar year 2025.

2. Materials and Methods

The CNM is investigating invasive isolates of *N. meningitidis* as well as native clinical specimens derived from normally sterile body sites.

Isolates are sub-cultured overnight on chocolate agar plates. The identification is confirmed by PCR using the *N. meningitidis*-specific targets *ctrA*, *sodC*, *tauE, metA*, and *shlA*. Serogroups are assessed by PCR as well as by commercial agglutination kits: A, B and C (Pastorex Meningitis, Bio-Rad) and W135, X, Y, Z and Z' (Difco Neisseria Meningitidis Antisera, Becton Dickinson).

Sequence analysis is performed on each isolate in two variable regions of the gene encoding the antigenic outer membrane protein porin A (*porA*-VR1 and *porA*-VR2) and in one variable region of the *fetA* gene (*fetA*-VR) encoding another outer membrane protein exhibiting sequence data which can be useful for tracing clones emerging or circulating in local populations (World Health Organization Manual – Laboratory Methods

for the Diagnosis of Meningitis caused by *Neisseria meningitidis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*).

In addition, multilocus sequence typing (MLST) is carried out on each isolate according to protocols recommended by the EMGM (http://emgm.eu). This approach is targeting variable regions of seven house-keeping genes (*abcZ*, encoding a putative ABC transporter; *adk*, adenylate kinase; *aroE*, shikimate dehydrogenase; *fumC*, fumurate dehydrogenase; *gdh*, glucose-6-phosphate dehydrogenase; *pdhC*, pyruvate dehydrogenase subunit, and *pgm*, phophoglucomutase). Each isolate is classified according to its multilocus genotype designated as a sequence type (ST), which is the combination of its alleles over the seven genetic loci tested. STs can be further grouped into clonal complexes (CC), which are defined in the *Neisseria* MLST profile database as groups of STs that share at least four of the seven loci in common with a central ST (http://pubmlst.org/neisseria/).
Isolates are then classified based on a combination of serotyping and molecular typing data according to the following scheme:
Serogroup : *porA*-VR1, *porA*-VR2 : *fetA*-VR : MLST (ST or/and CC).

The antimicrobial susceptibility testing is performed for each isolate using Mueller-Hinton agar + 5% defibrinated horse blood and 20 mg/L β-NAD (MH-F, bioMérieux). Minimum inhibitory concentrations (MICs) are determined for penicillin, ceftriaxone, meropenem, ciprofloxacin, minocycline and rifampicin by E-test strips (AB Biodisk, bioMérieux). The MICs are interpreted according to the current breakpoints recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST, www.eucast.org).

In case of no growth of the strain, clinical specimens are analyzed by qPCR to screen for *N. meningitidis* DNA, and if present, we assess the occurrence of the main serogroups by amplifying their corresponding genetic targets. Nucleic acids extraction from clinical specimens such as cerebrospinal fluid and EDTA blood is performed using the MagPurix 12 Nucleic Acid Extraction System (Zinexts Life science; Taiwan). DNA is amplified by real-time PCR to screen for the presence of the *N. meningitidis*-specific targets described above (panel has been completed based on Diene *et al*, 2016). PCR assays targeting the polysialyltransferase (*siaD*) gene are performed to assign *N. meningitidis*-positive specimens to serogroups B, C and Y/W; assignment to serogroup A is achieved by a

qPCR assay targeting the *sacC* gene. Finally, the differentiation between serogroups Y and W is asessed by the amplification of the *synF* (Y) and *synG* genes (W) [22].

3. Strain collection

The CNM stores all the received invasive meningococcal isolates at -80°C. The collection currently includes more than 500 isolates (between 2009 and 2025). Previous strains were also stored but their recovery by culture cannot be guaranteed (n=1'914 isolates between 1989 and 2009).

4. National and International quality assurance

There is currently no international quality assurance pertaining to meningococci. We are actively scouting whether this service would become available.

5. Epidemiological research

The precision of NGS permitted us to identify several independent monoclonal outbreaks related to *N. meningitidis* W135 that occurred between 2010 and 2016 in Switzerland. Our meta-analyses included samples from other previously published works and allowed establishing connections between Swiss MenWs and other European outbreaks as published recently in the Journal of Infection [23]. This project was made possible through a specific grant from SFOPH (Decision 16.928412).

We have analyzed the molecular epidemiology of *N. meningitidis* W (MenW) between 2017 and 2018 in Switzerland. In this period, we reported the circulation of three main MenW lineages: the Hajj-related, South American and ST-9316. While the first two lineages are part of the same clonal complex 11 and were already present in Switzerland, ST-9316 was new and emerged in 2018 in the canton of Vaud.

We highlighted that the distribution of ST-11 CC lineages was quite heterogenous without a precise geographical localization. We identified several outbreaks that occurred in 2017-2018 due to ST-11 CC lineages. In particular, we observed that some of these outbreaks were sub-variants of already circulating strains. Monitoring the current situation by WGS is strongly recommended as the heterogeneity of circulating lineages detected so far can favor the evolution and emergence of new strains.

Acoording to our analyses, the WGS represents the only technique that can allow to capture a detailed nation-wide epidemiological picture of a complex species like *Neisseria meningitidis*.

6. Additional meningococcal research

We published recently two papers:

Borrow R, Campbell H, Caugant DA, Cherkaoui A, Claus H *et al.* Global Meningococcal Initiative: Insights on antibiotic resistance, control strategies and advocacy efforts in Western Europe. Journal of Infection 89 (2024) 106335 / https://doi.org/10.1016/j.jinf.2024.106335

Lutz N, Lazarevic V, Gaïa N, Cherkaoui A, and Schrenzel J. Primary meningococcal arthritis by a nonencapsulated *Neisseria meningitidis* strain. *Clinical Microbiology and Infection 2025* / https://doi.org/10.1016/j.cmi.2025.02.005

7. Advisory service and Networking

7.1 Advisory service

Molecular testing:

We systematically conduct molecular assays to define the serogroups using isolates or directly from clinical specimens when the bacterial growth is not possible (or suspicion thereof). As mentioned above, it is likely that the true incidence of invasive *N. meningitidis* infection is missed by rapid empiric therapy (precluding successful cultivation), nor to mention the new clinical presentations related to MenW such as pneumoniae (typically undetected and not referred to the CNM unless presenting with a bacteraemia and thus fulfilling the current definition of invasive infection). Our current molecular approach covers the most frequent serotypes and a result can usually be communicated to the clinicians.

7.2 Networking

We have established contact with the Italian reference center for meningococci to further analyze our peculiar MenW epidemics, in conjunction with their national epidemiology. We do also have ongoing contacts with the French reference center.

7.3 Website

The dedicated website (www.meningo.ch) was fully rebuilt in 2018, and is available in French, German, Italian and English. We are currently updating it to better display the information.

8. Results

8.1. Phenotypic and molecular characterization

During the calendar year 2025, the CNM has received a total of 33 invasive isolates of *N. meningitidis*. These strains were isolated from blood cultures (n=29), cerebrospinal fluid (n=1), joint fluid aspiration (n=1), and iliac muscle abscess (n=1). In addition, a qPCR assay was performed on one CSF because there was no growth of the strain (Figure-1). Figure-2 depicts the number of *N. meningitidis* strains isolated in 2025 according to gender and serogroups.

Since 2014, the number of invasive meningococci isolated was increasing (Figure 3). However, in 2021 and 2022, the number of invasive *N. menigitidis* isolates was very low compared to previous years. Similar to 2020, this downward trend already observed in 2019 was deeply magnified by the sanitary situation linked to Sars-CoV-2. Invasive meningococcal disease cases in the Switzerland have then increased moderately since 2021. We have not yet reached the pre-pandemic levels. In 2024, 37 confirmed IMD cases were reported in Switzerland, of which we received 33 isolates and one CSF specimen (89%, 33/37).

The last decade has however witnessed considerable changes in the epidemiology of invasive meningococcal infections in Switzerland. In 2025, the MenB was the most frequently invasive serogroup (14/33; 42%), followed by MenY (12/33; 36%), MenW (6/33; 18%), and MenC (1/33; 3%) (Figure 4 and Figure 5).

Figure-6 depicts the number of *N. meningitidis* strains collected in 2025 and classified by serogroups and age groups.

Figure 7 shows the distribution of serogroups by geographical regions in 2025.

Table 1 and Figure 8 depict the molecular characterization using MLST of the 33 Nmen strains analyzed in 2025. The two MenW strains isolated in the joint fluid aspiration and the iliac muscle abscess specimens belong to ST-23 CC.

8.2. Antimicrobial Susceptibility Testing

Table 2 depicts the antimicrobial susceptibility profiles and the MICs ranges by drugs, with the MIC_{50} and MIC_{90} of the 33 invasive *N. meningitidis* strains referred to the Swiss National Reference Center for meningococci in 2025. Applying the EUCAST breakpoints (v15.0; 2025), all invasive *N. meningitidis* strains tested revealed susceptible to ceftriaxone, meropenem, minocycline and rifampicin.

Among the 33 invasive *N. meningitidis* strains identified in 2025, three strains exhibited resistance to ciprofloxacin and/or penicillin:

- One MenB strain, ST-191, resistant to penicillin (MIC = 0.5mg/l) and ciprofloxacin (MIC = 0.125mg/l). The molecular analysis of this strain showed the presence of mutations in the five critical residues of PBP2 (F504L, A510V, I515V, H541N, and I566V) and the presence of the altered *gyrA* allele (*gyrA* T91I mutation);
- One MenY strain, ST-4044, resistant to penicillin (MIC = 0.5mg/l).
- One MenY strain, ST-3587, harboring bla_{ROB-1} (Penicillin MIC = 16mg/l);

Summary of key observations

- Invasive meningococcal disease cases in Switzerland have increased moderately since 2021. We have not yet reached the pre-pandemic levels. In 2025, MenB was the most frequent invasive serogroup (14/33; 42%), followed by MenY (12/33; 36%), MenW (6/33; 18%), and MenC (1/33; 3%).
- All invasive *N. meningitidis* strains identified in 2025 were susceptible to ceftriaxone, meropenem, minocycline and rifampicin.
- One MenB strain, ST-191, resistant to penicillin (MIC = 0.5mg/l) and ciprofloxacin (MIC = 0.125mg/l). The molecular analysis of this strain showed the presence of mutations in the five critical residues of PBP2 (F504L, A510V, I515V, H541N, and I566V) and the presence of the altered *gyrA* allele (*gyrA* T91I mutation);
- One MenY strain, ST-3587, harboring $bla_{\text{ROB-1}}$ (Penicillin MIC = 16mg/l);
- One MenY strain, ST-4044, resistant only to penicillin (MIC = 0.5mg/l).
- In France, MenB ST-485 was identified in three IMD cases detected during February 2025 (linked to the ski station Morzine).
- 2025 : MenB ST-485 was not identified in Switzerland.
    - 2023/2024 : MenB ST-485 was identified in two patients:
        - 2023 : a 62 years old (F) - sample: CSF
        - 2024 : 63 years old (M) - samples: CSF and blood culture

9. Discussion

As of early 2025, IMD incidence in Switzerland remained stable, with an average of about 50 cases reported annually (approx. 0.6/100,000 inhabitants), consistent with the 2011–2020 average. In 2025, 37 IMD cases were reported to the SFOPH. We have not reached the pre-pandemic levels. The incidence in 2023 has exceeded the level recorded in 2020 (0.38 *versus* 0.23 in 2020), and has even doubled when compared to 2022 (0.38 *versus* 0.19 in 2022). The incidence of IMD in 2024 was 0.39 for 100,000, which corresponds to 35 cases reported. The proportion of MenY among the invasive strains in 2024 has increased considerably compared to 2022; 52% (14/27) versus 17% (2/12), and exceeded the peak observed in 2018 (12 IMD cauded by MenY). In 2025, 12 IMD caused by MenY were reported (12/33; 36%). MenB was the most frequently invasive serogroup (14/33; 42%).

N. meningitidis ROB-1 β-lactamase producer, MenY, was identified in Aargau from the joint fluid aspiration of a 78-year-old female.

N. meningitidis with *the* altered *gyrA* allele (*gyrA* T91I mutation), MenB, was identified in Basel-Stadt from the blood culture of a <1-year-old male. This strain was also resistant to penicillin.

The monitoring and follow-up of the ciprofloxacin-and penicillin-resistant *N. meningitidis* strains among the invasive and the colonizer strains should be systematically pursued.

Across Western Europe, the incidence of IMD is still low (Table-2). Men B remains the foremost recovered serogroup. Nevertheless in the last few years, MenY and MenW cases have emerged in some EU countries like Switzerland. Very recently, an outbreak of Men B was reported in Rennes, France, prompting for a large scale immunization campaign after NGS confirmed a clonal outbreak.

All the 33 Nmen strains isolated in 2025 were submitted to Public databases for molecular typing and microbial genome diversity (https://pubmlst.org/organisms/neisseria-spp/submissions).

10. Acknowledgements

The authors thank the Laboratory of Bacteriology for excellent assistance, and the SFOPH for financial and scientific support.

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Figures

Figure 1. Number of *N. meningitidis* identified in 2025 according to the age of the patients and the specimen types.

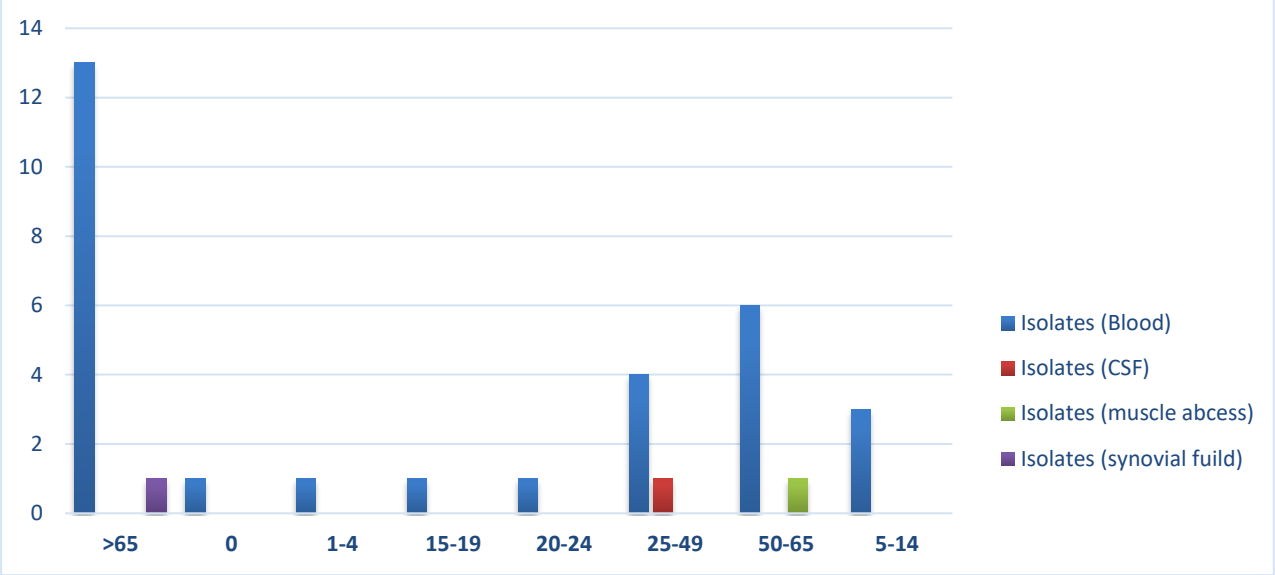

Figure 2. Number of *N. meningitidis* strains isolated in 2025 according to gender and serogroups.

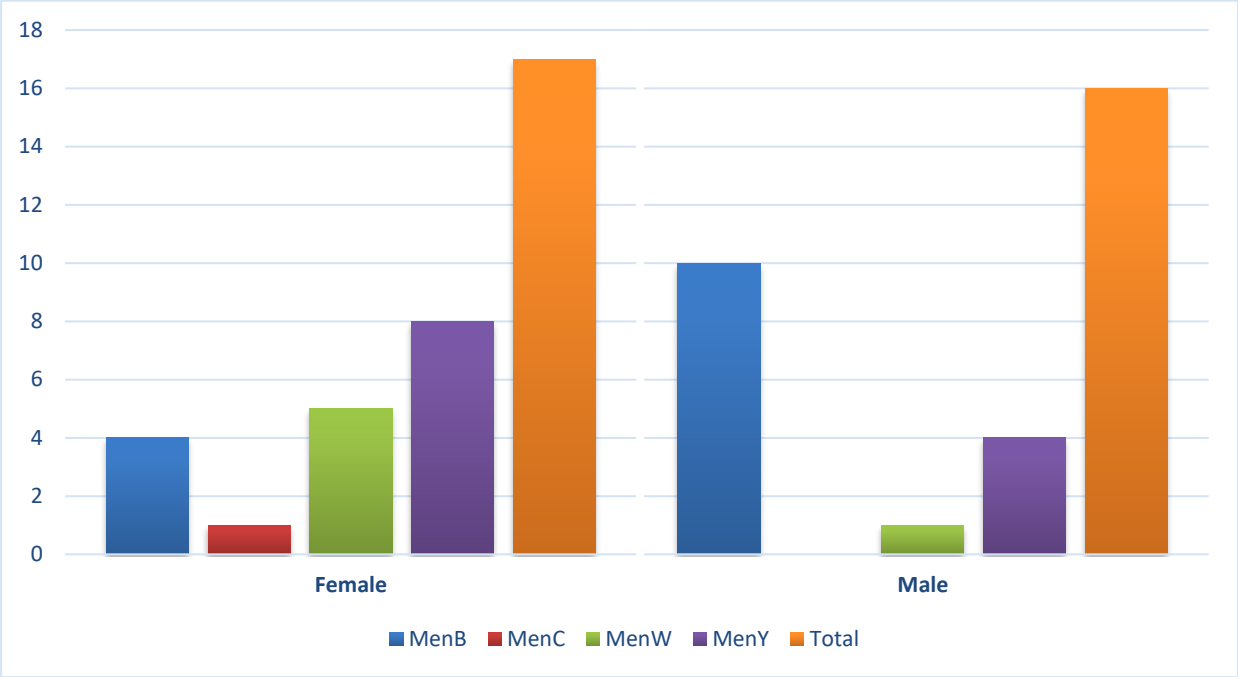

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Figure 3. Annual number of cases of invasive meningococcal diseases reported to the Swiss Federal Office of Public Health (SFOPH) and number of *N. meningitidis* strains referred to the Swiss National Reference Center for Meningococci (SNRCM) from 2009 to 2025

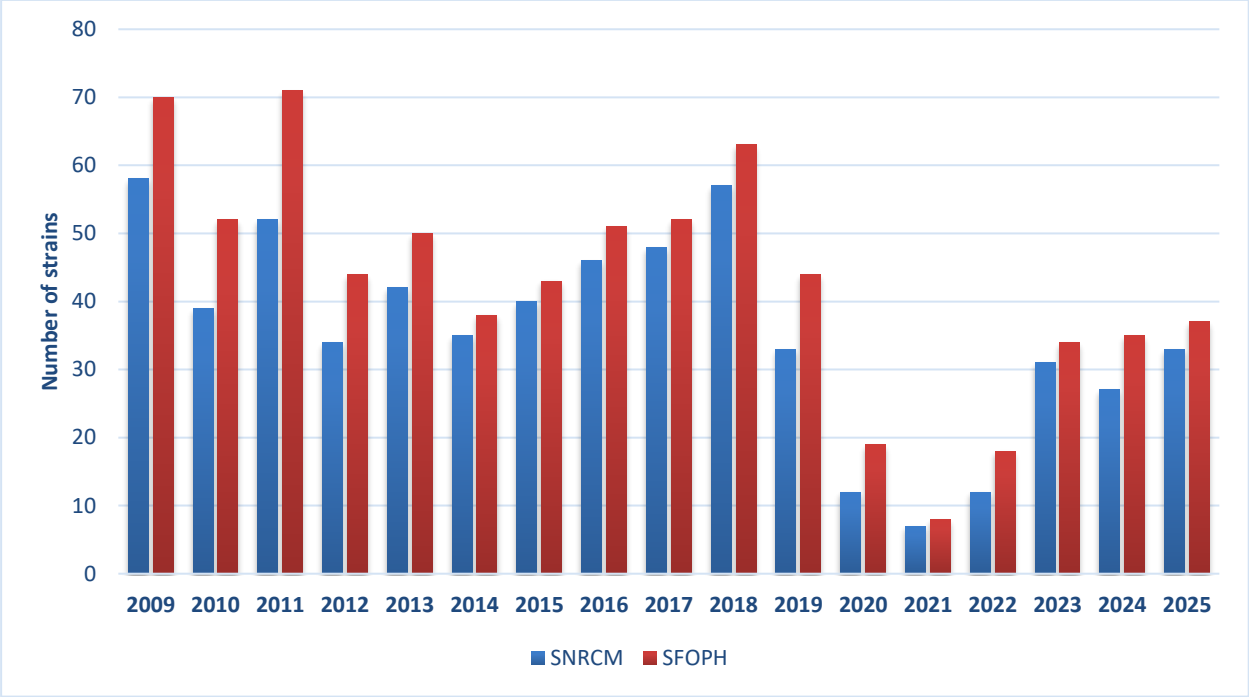

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Figure 4. Serogroups distribution in 2025 (n=33)

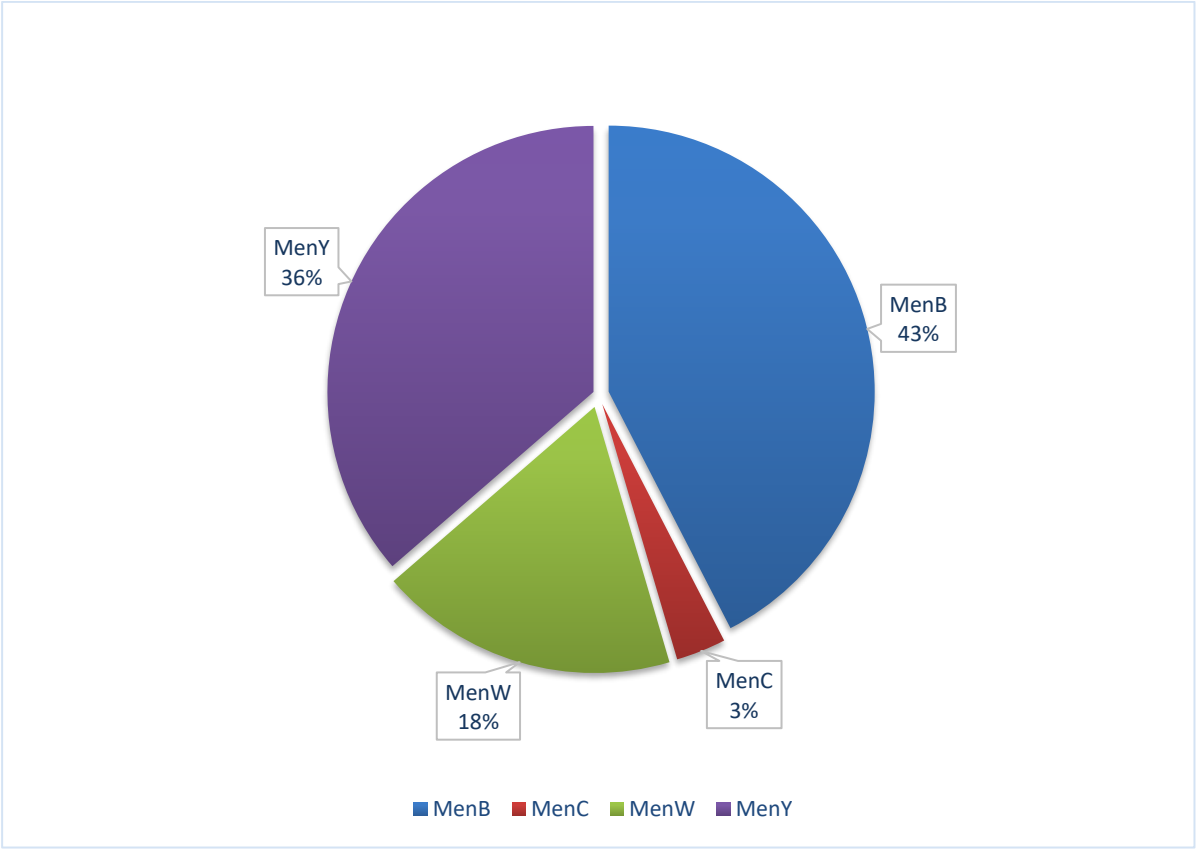

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Figure 5. Annual number of strains representing the main serogroups B, C, X, Y and W of invasive *N. meningitidis* as determined at the Swiss National Reference Center for meningococci from 2009 to 2025

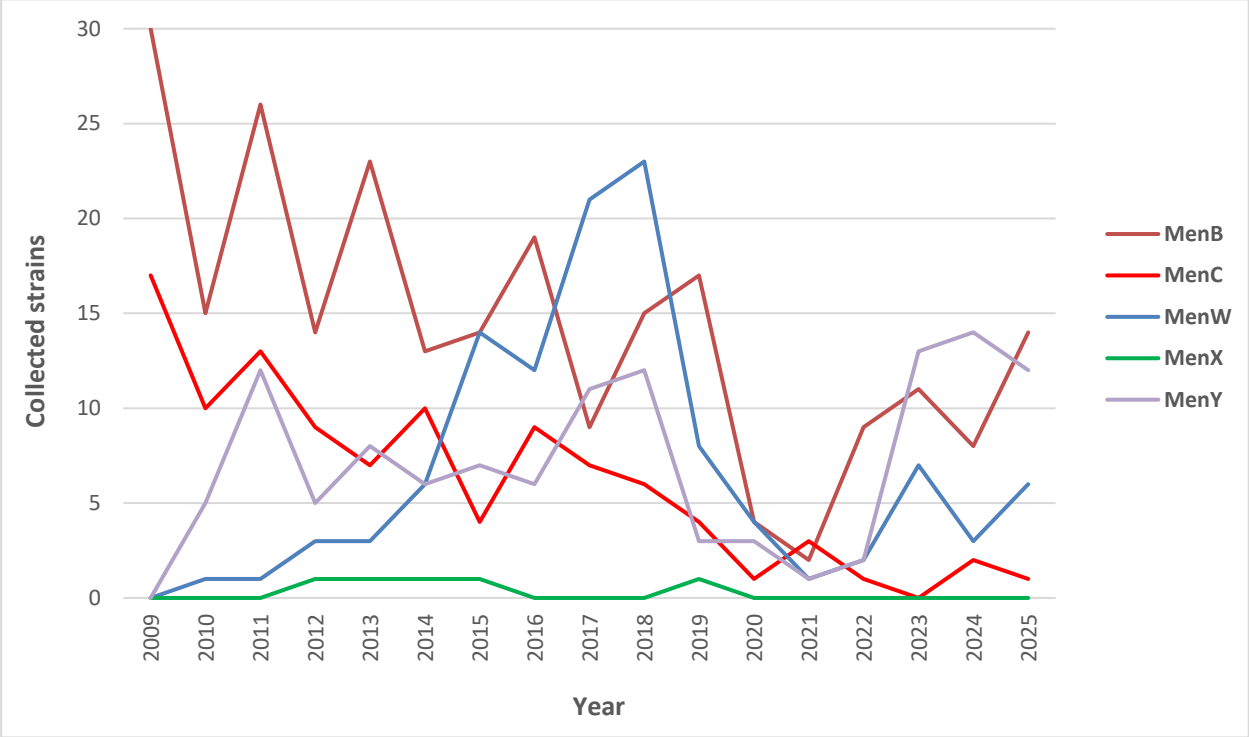

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Figure 6. Number of *N. meningitidis* strains isolated in 2025 according to age and serogroups.

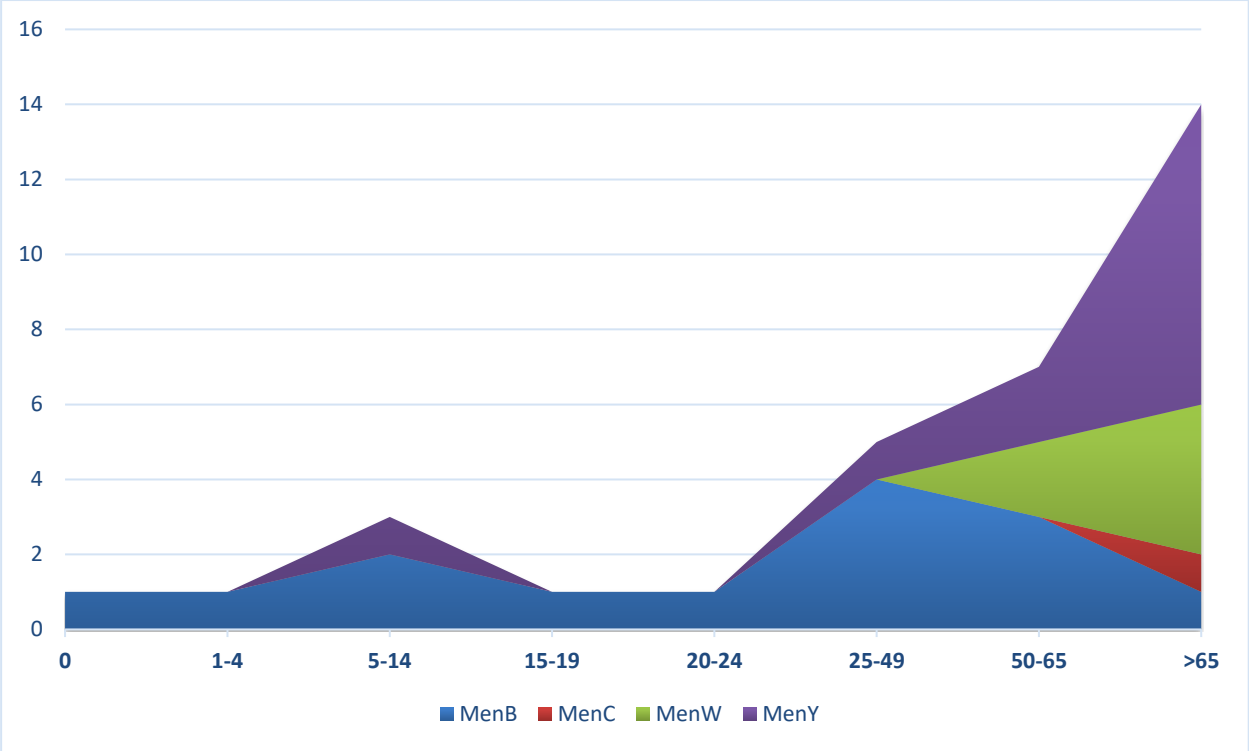
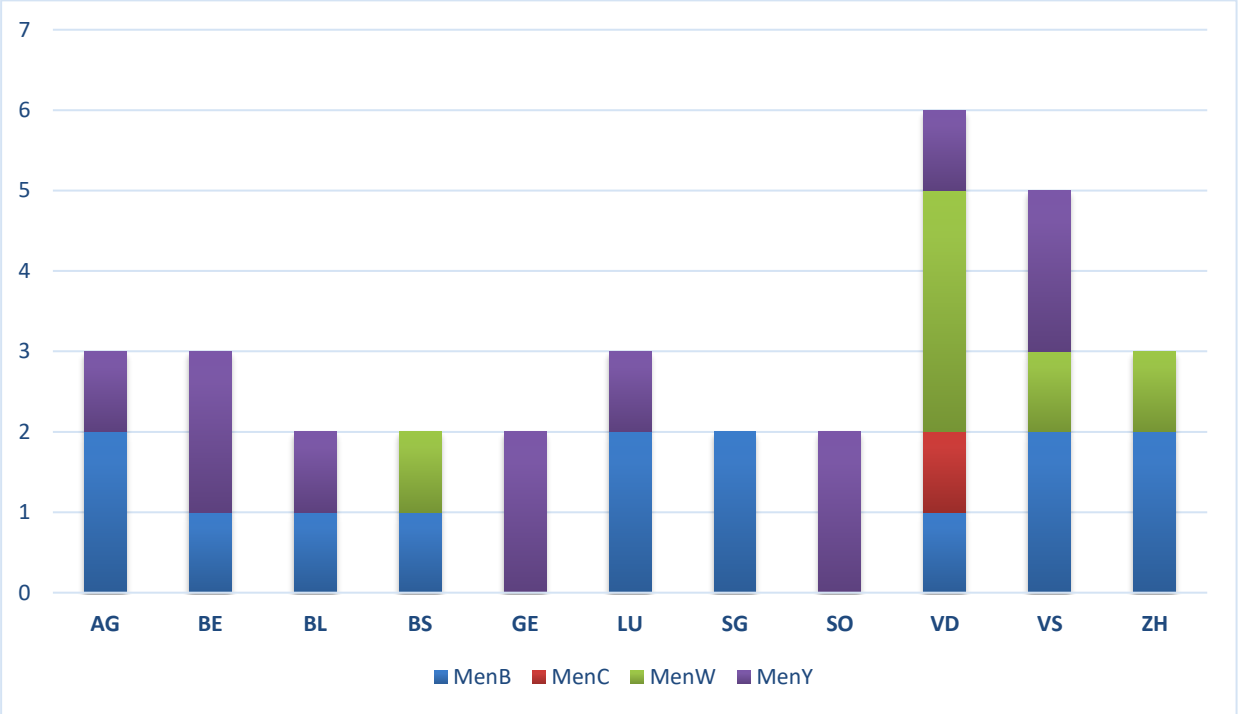


Figure 7. Distribution of serogroups by geographical regions in 2025



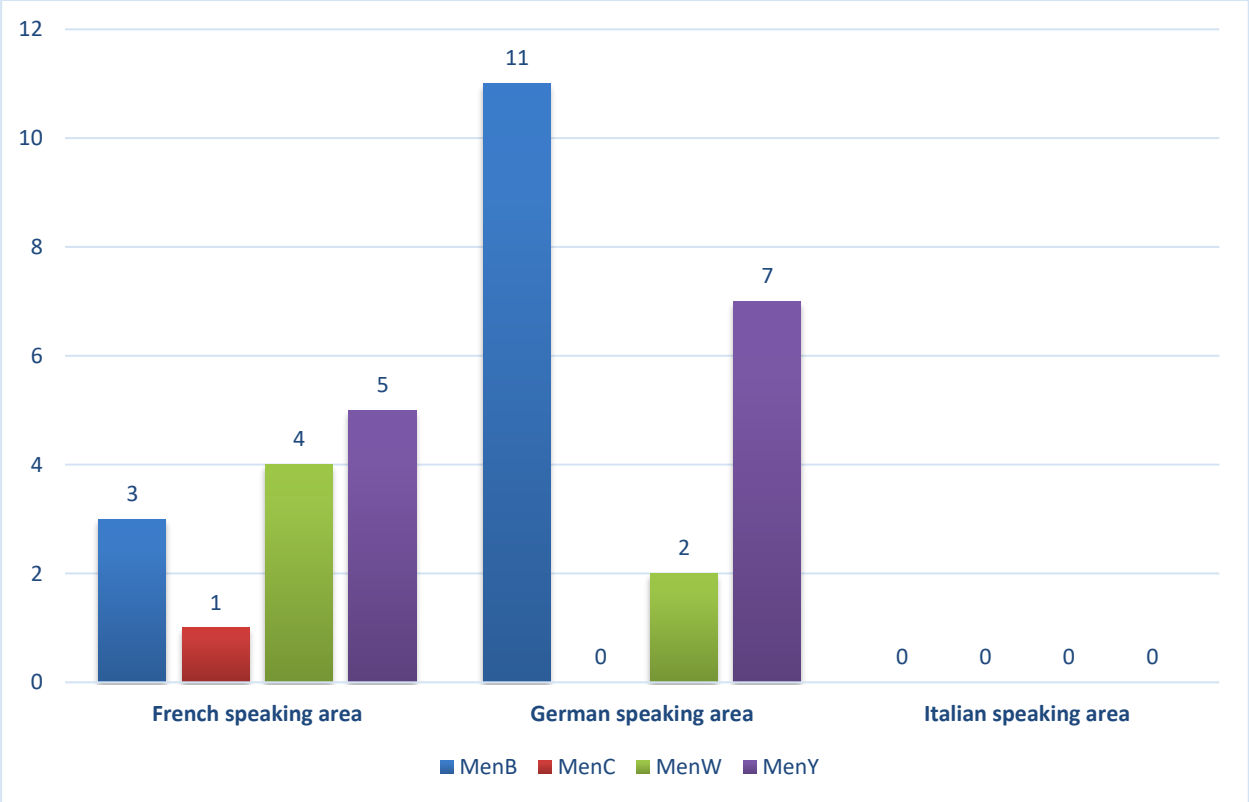


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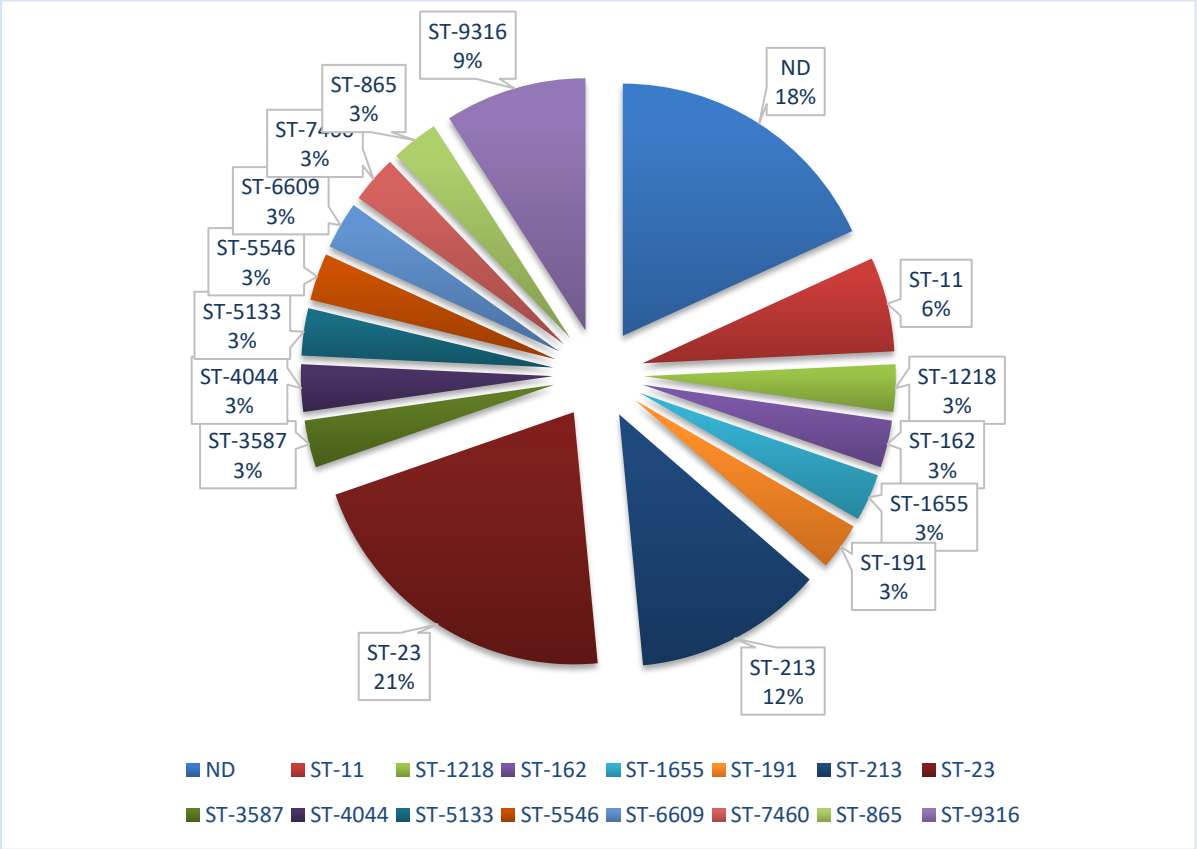
Figure 8. Distribution of sequence types in 2025



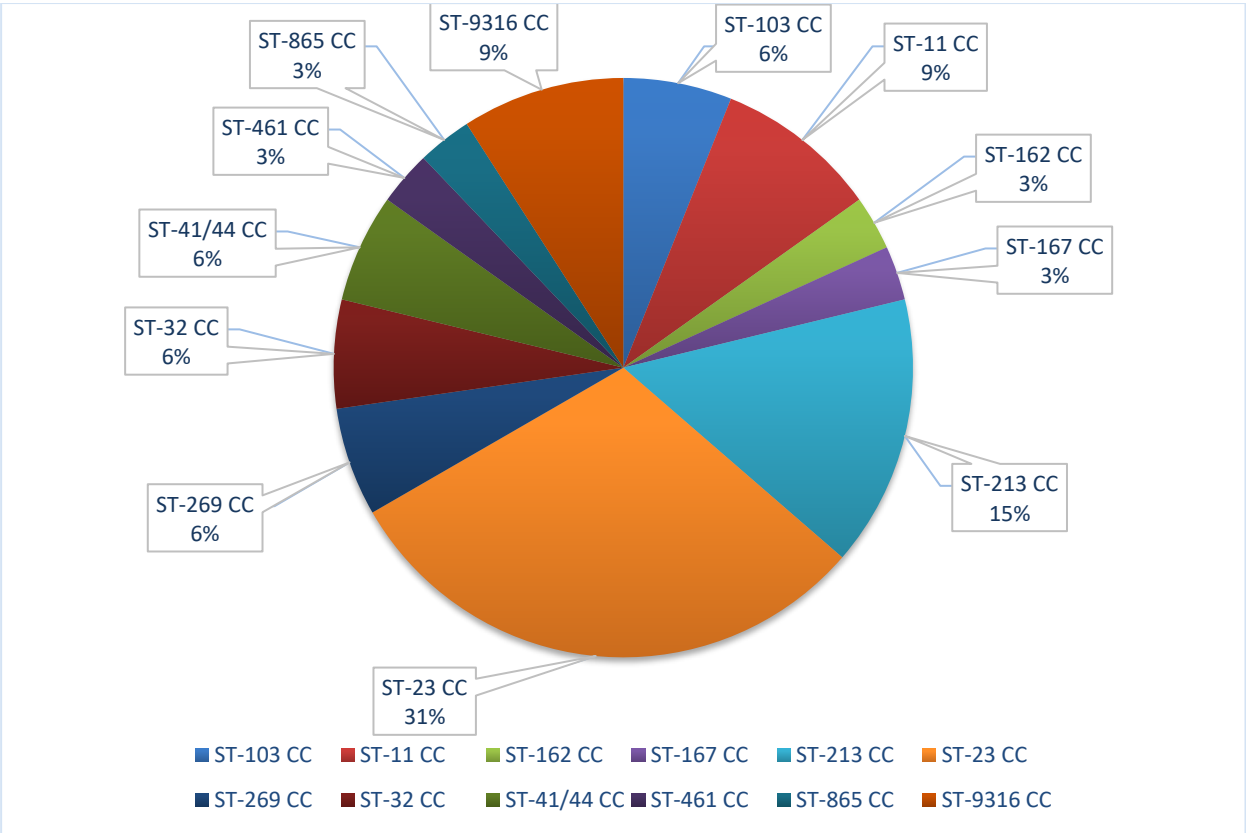


Table 1. Synopsis of MLST profiles and serogroups of invasive *N. meningitidis* strains referred to the Swiss National Reference Center for meningococci in **2025**

Specimen	Canton	Serogroup	Sequence types (STs)	Clonal complex
Blood culture	AG	**MenB**	ST-162	ST-162 CC
Blood culture	BS	***MenB**	ST-191	ST-41/44 CC
Blood culture	ZH	**MenB**	ST-213	ST-213 CC
Blood culture	AG	**MenB**	ST-213	ST-213 CC
Blood culture	VS	**MenB**	ST-213	ST-213 CC
Blood culture	BL	**MenB**	ST-213	ST-213 CC
Blood culture	LU	**MenB**	ST-865	ST-865 CC
Blood culture	SG	**MenB**	ST-1218	ST-213 CC
Blood culture	LU	**MenB**	ST-6609	ST-269 CC
Blood culture	BE	**MenB**	ST-7460	ST-32 CC
Blood culture	ZH	**MenB**	ND	ST-32 CC
Blood culture	SG	**MenB**	ND	ST-41/44 CC
Blood culture	VD	**MenB**	ND	ST-461 CC
Cerebrospinal fluid	VS	**MenB**	ND	ST-269 CC

* MenB strain, ST-191, resistant to penicillin (MIC = 0.5mg/l) and ciprofloxacin (MIC = 0.125mg/l).

Specimen	Canton	Serogroup	Sequence types (STs)	Clonal complex
Blood culture	VD	**MenC**	ST-5133	ST-103 CC

Specimen	Canton	Serogroup	Sequence types (STs)	Clonal complex
Blood culture	ZH	**MenW**	ST-11	ST-11 CC
Blood culture	VD	**MenW**	ST-11	ST-11 CC
Blood culture	BS	**MenW**	ST-9316	ST-9316 CC
Blood culture	VD	**MenW**	ST-9316	ST-9316 CC
Blood culture	VS	**MenW**	ST-9316	ST-9316 CC
Blood culture	VD	**MenW**	ST-4044	ST-11 CC

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Specimen	Canton	Serogroup	Sequence types (STs)	Clonal complex
Blood culture	BE	**MenY**	ST-23	ST-23 CC
Blood culture	BE	**MenY**	ST-23	ST-23 CC
Blood culture	VD	**MenY**	ST-23	ST-23 CC
Blood culture	BL	**MenY**	ST-23	ST-23 CC
Blood culture	SO	**MenY**	ST-23	ST-23 CC
Blood culture	GE	**MenY**	ST-23	ST-23 CC
Blood culture	SO	**MenY**	ST-23	ST-23 CC
Blood culture	VS	**MenY**	ST-1655	ST-23 CC
Joint fluid	AG	***MenY**	**ST-3587**	**ST-23 CC**
Blood culture	GE	**MenY**	ST-5546	ST-103 CC
iliac muscle abscess	LU	**MenY**	ND	ST-23 CC
Blood culture	VS	**MenY**	ND	ST-167 CC

* MenY strain, **ST-3587**, harbouring ***bla***$_{ROB-1}$ (Penicillin MIC = 16mg/l).

Table 2. Antimicrobial susceptibility testing (EUCAST breakpoints) of the 33 invasive *N. meningitidis* strains referred to the Swiss National Reference Center for meningococci in 2025

Drugs	Range	Minimum inhibitory concentration (MIC)		Breakpoint susceptible (≤ µg/ml)	% of strains considered susceptible
		MIC_{50}	MIC_{90}		
Penicillin	0,006-16	0.094	0.25	0.25	90.9
Ceftriaxone	0,002-0,003	0.002	0.002	0.125	100
Meropenem	0,003-0,094	0.012	0.047	0.25	100
Ciprofloxacin	0,002-0,125	0.003	0.004	0.016	97.0
Minocycline	0,023-0,5	0.19	0.38	1	100
Rifampicin	0,002-0,125	0.016	0.064	0.25	100

Red: increase (resistance) vs 2024

Green: decrease (resistance) vs 2024

Black, identical to 2024