Region Örebro County

NRL *Neisseria meningitidis*, Department of Laboratory Medicine, Örebro University Hospital

Annual Report for the National Reference Laboratory for *Neisseria meningitidis*, 2025

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Background

Cases of invasive meningococcal disease in Sweden are reported through the communicable disease surveillance system, Sminet, by both laboratories and treating physicians. Bacterial isolates, as well as culture-negative but PCR-positive samples (primarily cerebrospinal fluid), are sent to the National Reference Laboratory (NRL, National Reference Laboratories) at Örebro University Hospital.

At the NRL, identification, serological and/or genetic grouping is performed on invasive *Neisseria meningitidis* isolates, and upon request on non-invasive isolates. Typing is carried out using whole genome sequencing (WGS) on all culture-positive invasive isolates. Antimicrobial susceptibility testing is performed using MIC determination. For culture-negative samples from normally sterile sites, PCR diagnostics; genogrouping, and genosubtyping are performed. The laboratory monitors epidemiology nationally and globally, as well as developments in knowledge and methodology within the field.

Epidemiology of *Neisseria meningitidis* 2025

During 2025, 41 cases of invasive meningococcal disease were reported in Sweden, corresponding to an incidence of 0.4 cases per 100,000 people (see Figure 1). The incidence of invasive meningococcal disease declined sharply during the COVID-19 pandemic. Since then, the incidence has increased but has not yet reached the levels observed in the years before the pandemic.

At the NRL, material (isolates or clinical specimens) was received from all reported invasive cases during 2025, including 39 isolates and 2 cerebrospinal fluid samples from culture-negative cases. The isolates were obtained from blood (n=29), cerebrospinal fluid (n=7), and synovial fluid (n=3).

The distribution of serogroups among the culture-positive cases were Y (n=19), B (n=10), W (n=8), and C (n=2). The two culture-negative samples were genogrouped as B (n=2).

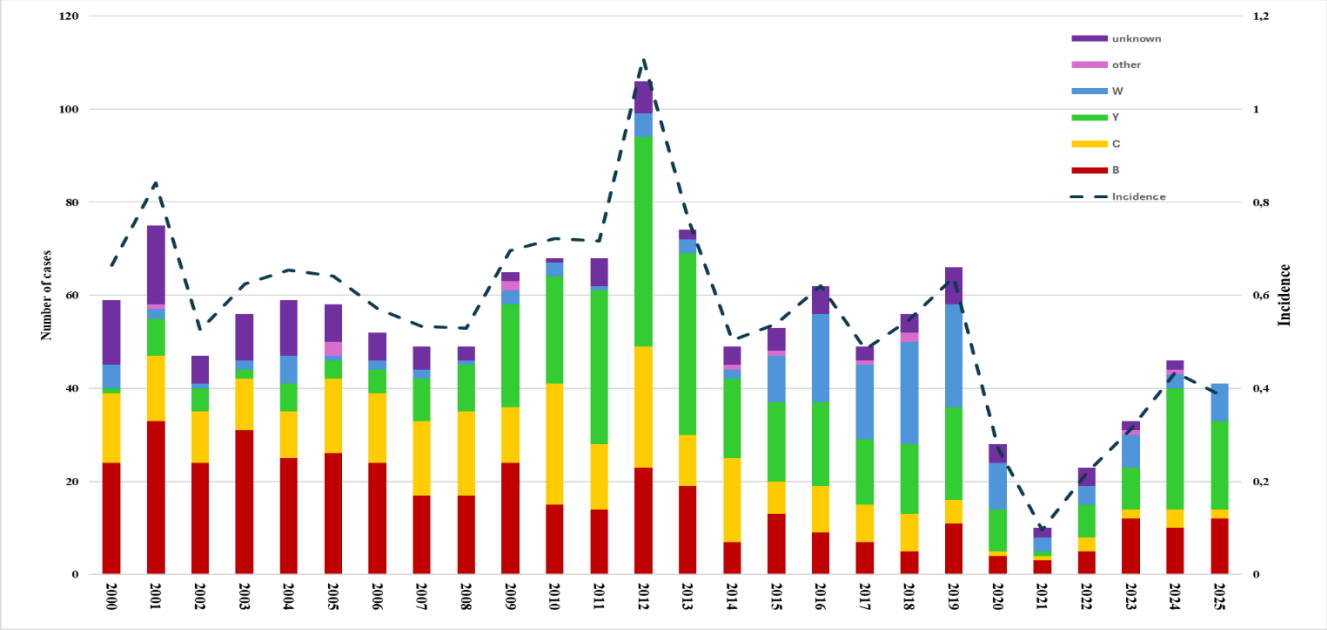

Figure 1. Number of cases, serogroup distribution, and incidence (number of cases per 100,000 people) of invasive meningococcal disease in Sweden during 2000–2025.

The median age among the cases was 49 years (range 0–94 years), with the highest number of cases reported in the age group ≥80 years (n=7), see Figure 2. Compared with previous years, a slight increase in cases was observed in the 40–49 years age group (n=5), where 3 of the cases were caused by serogroup B (see Figure 2). The majority of cases were reported among women (61%, 25/41). Of the reported cases during 2025, three individuals died, corresponding to a mortality rate of 7% (source: Epidemiological Annual Report, Public Health Agency of Sweden).

MIC determination was performed on all culture-positive isolates. One isolate was resistant to benzylpenicillin (PcG), while the remaining isolates were susceptible to all tested antibiotics (PcG, cefotaxime, chloramphenicol, ciprofloxacin, rifampicin, and meropenem).

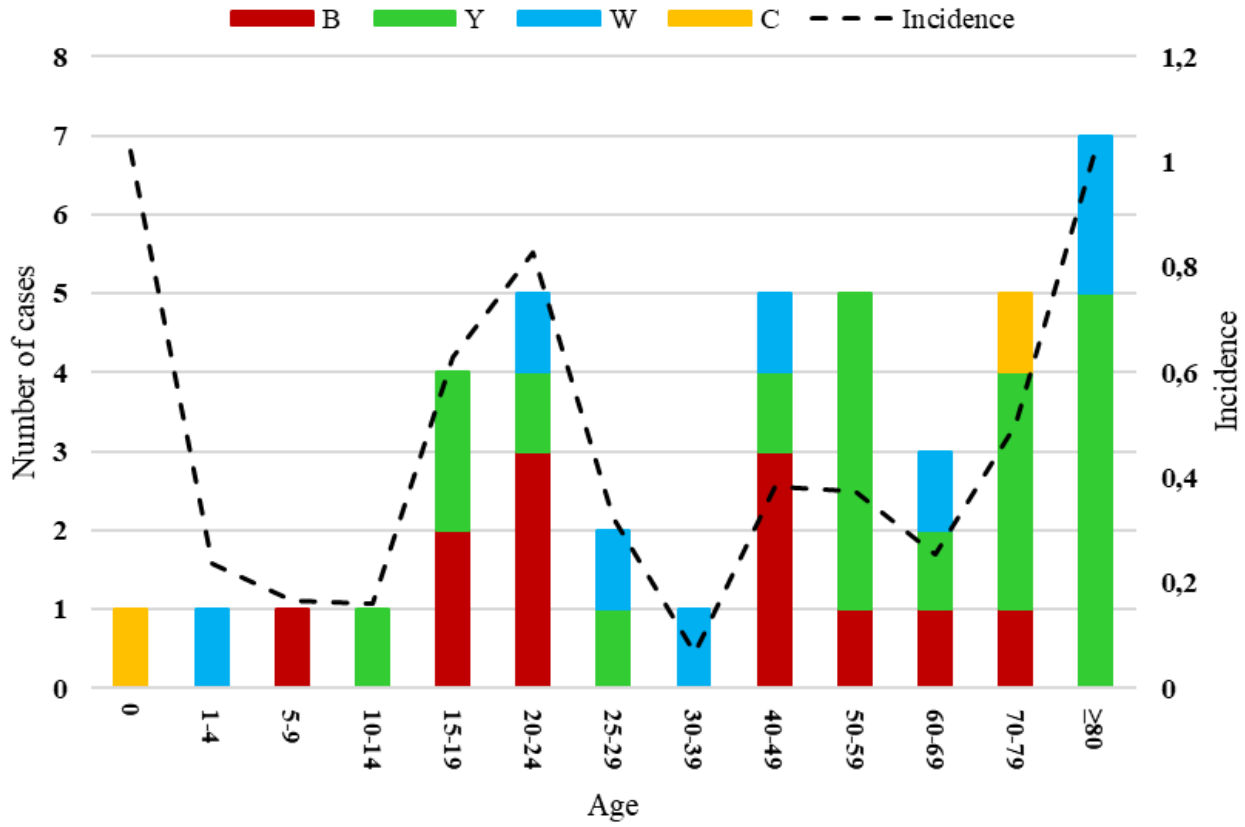

Figure 2. Distribution of invasive meningococcal disease and incidence (number of cases per 100,000 people) across different age groups, 2025.

Fine typing results (PorA VR1, VR2, *fetA*) for all culture-positive samples that underwent whole genome sequencing are presented in Table 1. The most common fine types during 2025 were P1.5-2:F1-1 (n=7), P1.5-1,2-2:F5-8 (n=5), and P1.5-2,10-1:F4-1 (n=5), which were found among serogroup W and Y isolates. This can be compared with the second most common serogroup (B), in which several different fine types were represented (Table 1). This suggests that the serogroup B cases observed during 2025 were not caused by specific genetic clusters but rather reflected more sporadic cases. Genosubtyping (*porA*) was not performed on culture-negative samples during 2025 due to technical issues with the method.

Table 1. Fine typing results for all whole genome sequenced *Neisseria meningitidis* isolates from 2025.

Finetype*	**B**	**C**	**W**	**Y**	**Total**
P1.5-2: F1-1			7		7
P1.5-1,2-2: F5-8				5	5
P1.5-2,10-1: F4-1				5	5
P1.5-2,10-1: F5-12				4	4
P1.5-1,10-4: F3-4				2	2
P1.5-2,10-1: F5-8	1		1		2
P1.22,14: F5-5	2				2
P1.19,15: F4-28	2				2
P1.5-1,10-1: F4-1				1	1
P1.5-1,10-62: F4-1				1	1
P1.5-2,10-23: F4-1				1	1
P1.5-1,10-8: F1-3		1			1
P1.19,15: F5-1	1				1
P1.18-1, 34: F1-5	1				1
P1.18-1,30-34: F3-3	1				1
P1.7,16-29: F3-3		1			1
P1.7-2,4: F1-5	1				1
P1.12-1,13: F1-66	1				1

*P1.PorA VR1, PorA VR2: fetA

Genetic differences among invasive *N. meningitidis* isolates from 2025 were analyzed using whole genome sequencing. All culture-positive samples (n=39) were whole genome sequenced and uploaded to the *Neisseria* PubMLST database (http://PubMLST.org/neisseria), an international public database for molecular typing and microbial diversity.

The relatedness between isolates is illustrated in Figure 3 as a network based on genetic differences in 1,329 core genes (cgMLST), according to the PubMLST database. The most common clonal complexes during 2025 were ST-23 complex (n=17), ST-11 complex (n=7), and ST-32 complex (n=5), see Figure 3.

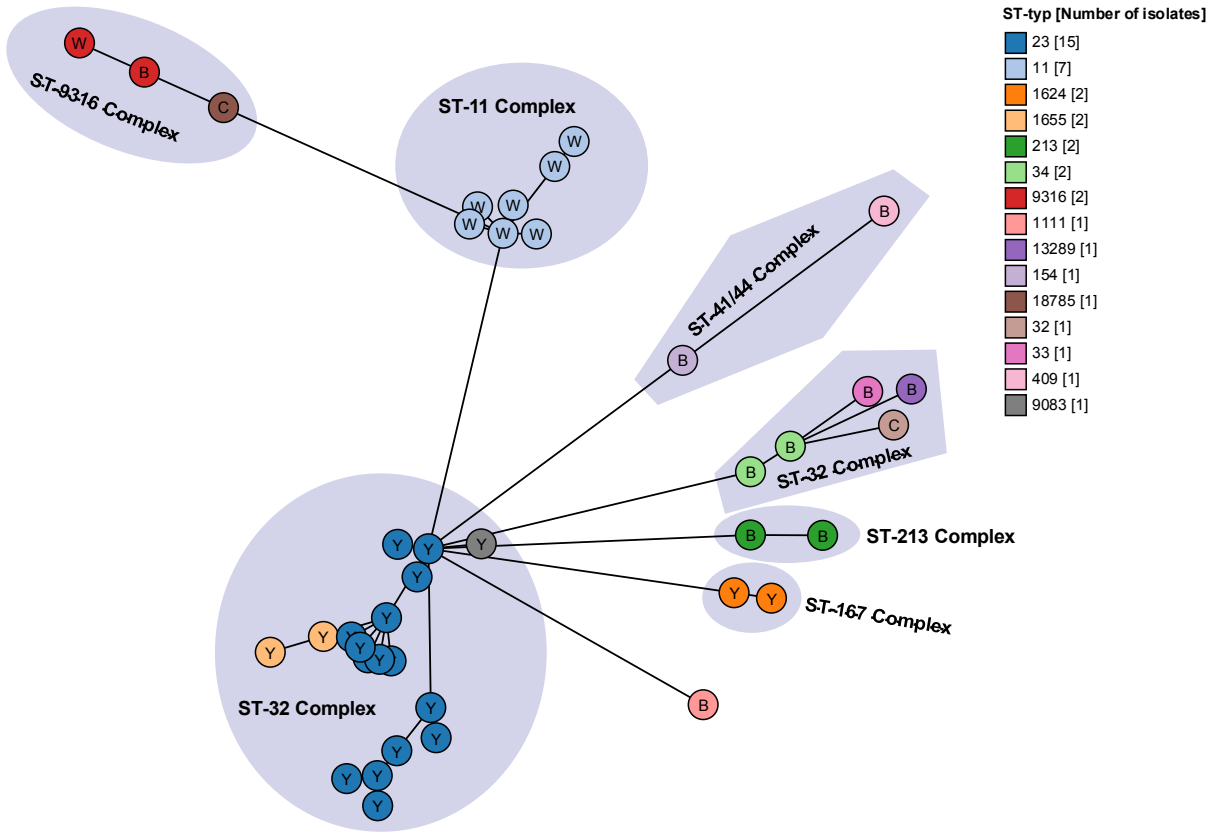

Figure 3. Whole genome sequenced *Neisseria meningitidis* isolates (n=39) from 2025. A core genome MLST (cgMLST) analysis was performed, based on genetic differences in 1,329 core genes (https://pubmlst.org/software/bigsdb). Each isolate is represented by a circle, with the serogroup indicated inside the circle. The circles are color-coded according to the ST type, and the clonal complexes are labeled in the figure. Genetic differences between the isolates are visualized by branch distances.

During 2025, five cases of invasive meningococcal disease caused by serogroup Y were reported from one region in Sweden. The isolates showed different fine typing results: P1.5-2,10-1:F4-1 (n=2), P1.5-2,2-2:F5-8 (n=2), and P1.5-2,10-1:F5-12 (n=1). The cases occurred between February and July 2025.Figure 4 shows a phylogenetic tree containing all serogroup Y isolates from Sweden in 2025. In the tree, isolates from this region are highlighted in red (PubMLST ID). Two of these cases were reported within 1.5 weeks of each other and clustered together in the tree with only 10 allelic differences, shown in Figure 4. The regional communicable disease control physician was contacted by the NRL, but no epidemiological link between the cases could be identified. The remaining isolates are clustered at different positions within the tree (Figure 4).

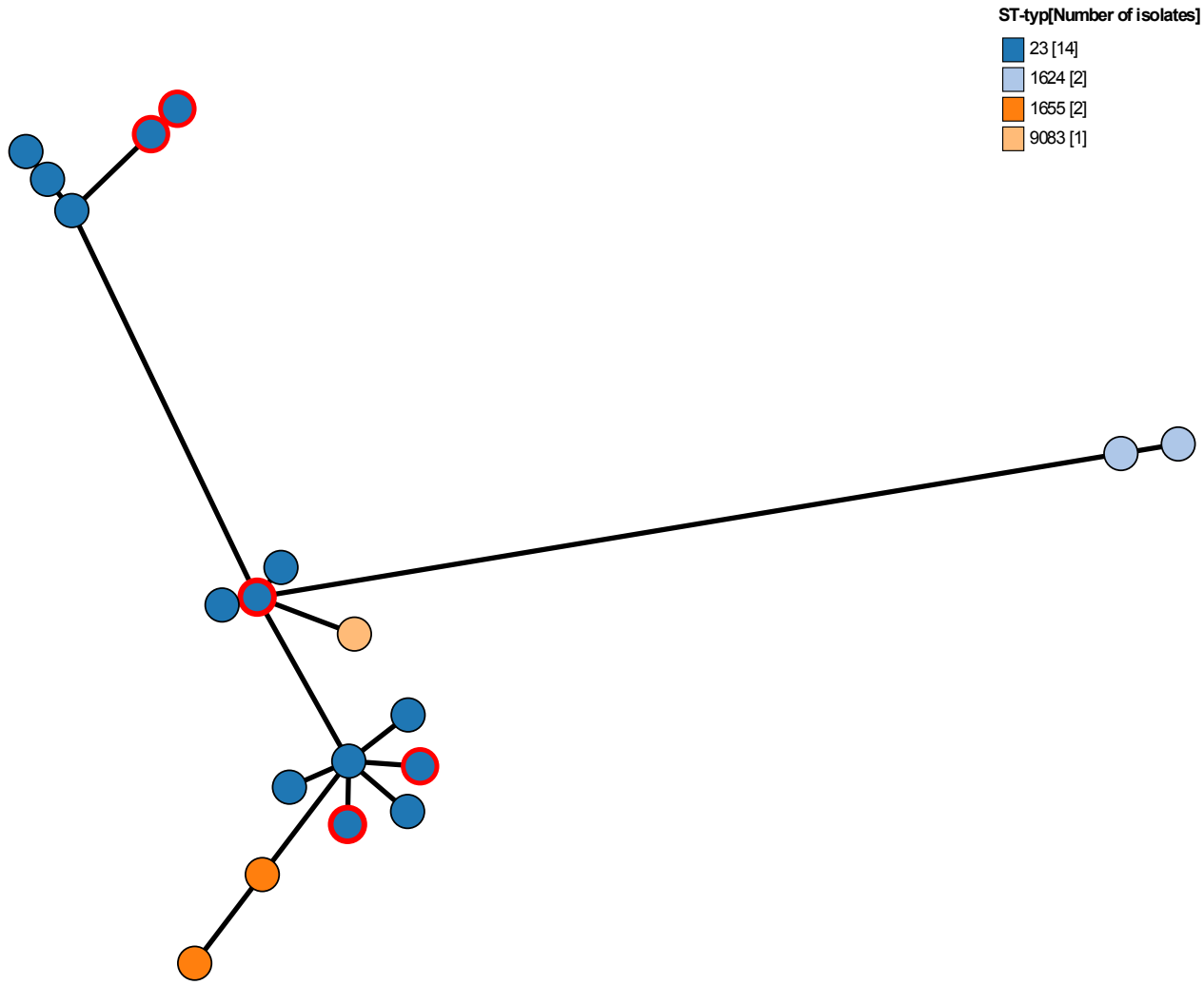

Figure 4. Whole genome sequencing of all Neisseria meningitidis isolates from 2025 belonging to serogroup Y, clonal complex 23 (cgMLST analysis; https://pubmlst.org/software/bigsdb). Each isolate is represented by a circle, and the color coding within the circles corresponds to the different ST types. Isolates marked with a red circle were collected from a region where several cases of serogroup Y were reported during 2025.

Methodological changes

Genosubtyping of culture-negative samples by Sanger sequencing was not performed during 2025 due to technical issues with the method. During 2025, development of a method for amplicon sequencing of the *porA* gene, approximately 700 bp (VR1–VR3), using Oxford Nanopore sequencing was initiated, with planned implementation in routine diagnostics during 2026.

During the year, development work was also carried out on a rapid method for whole genome sequencing using Oxford Nanopore technology to determine relatedness between isolates, which may be of major importance for contact tracing and outbreak investigations.

New reagents for serogrouping were evaluated during 2025 and will be introduced in 2026, as the previous reagents are no longer being manufactured.

Educational initiatives

A biomedical scientist was trained in *Neisseria* diagnostics during 2025.

An annual epidemiological report is published in collaboration with the Public Health Agency of Sweden, and resistance data are reported to Swedres.

During the Swedish annual meeting for infection and microbiology (SVIM), held in Örebro on 20–23 May 2025, two posters from the NRL were presented: one describing the NRL assignment and another on the national epidemiology of *Neisseria meningitidis* during 2023–2024. In addition, an oral presentation entitled "The microbiome in relation to carriage dynamics of *Neisseria meningitidis*" was delivered, as well as a symposium on "Bacterial meningitis with a focus on *Neisseria meningitidis*," featuring a moderator and a speaker from the NRL together with patient participation, which was highly appreciated.

In addition, telephone consultations were conducted with treating physicians and regional medical officers for communicable disease control.

Global Surveillance and Epidemiological Developments

Several European countries have continued to report an increase in *N. meningitidis* serogroup B. In Sweden the incidence of serogroup B has not increased, although it was the second most common serogroup in Sweden during 2025. Instead an increase in serogroup Y cases has been observed (see Figure 1).

During 2025, two staff members from the NRL participated in the 17th EMGM (The European Meningococcal Disease Society) in Crete, Greece, and contributed with two oral presentations: "Invasive meningococcal disease in Sweden 2023–2024" (P. Mölling) and "The microbiome in relation to *Neisseria meningitidis* carriage dynamics" (C. Klanger).

During 2025, the NRL also continued its active participation in the European reference network, the European Union Invasive Bacterial Diseases Laboratory Network (IBDLabNet).

The NRL, through P. Mölling and S. Jacobsson, also continued participation in the global laboratory network Invasive Respiratory Infections Surveillance (IRIS) Initiative during 2025, a network of reference laboratories from 30 countries across six continents. The initiative was initially established to monitor changes in invasive disease caused by *N. meningitidis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae* during the COVID-19 pandemic. The project has since continued to monitor the long-term impact of the COVID-19 pandemic on invasive bacterial infections.

Research

At the NRL, research on *N. meningitidis* is ongoing, with collaborations both nationally and internationally, including the following areas:

- Studying epidemiology over time, including changes in the distribution and incidence of serogroups
- Investigating *N. meningitidis* carriage and its interaction with other bacteria
- Studying the ability of *N. meningitidis* to cause disease in mice infected with isolates associated with invasive disease versus carriage
- Identifying genetic variants associated with invasive disease or carriage of *N. meningitidis*

At the NRL, PhD student Cecilia Klanger is supervised within the project *Genetic variants of Neisseria meningitidis linked to phenotypic outcome of infection vs carriage*.

An active research collaboration is conducted with Professor Muhamed Taha (Institut Pasteur, Paris, France), Professor Eva Särndahl and Associate Professor Alexander Persson (Örebro University), Associate Professor Edmund Loh (Karolinska Institutet), and Associate Professor Olof Hertting (Karolinska University Hospital), as well as their colleagues.

A bachelor's thesis was also supervised at the NRL during 2025, in which Ida Liljedahl described "Rapid whole genome sequencing for early outbreak detection of *Neisseria meningitidis*."

Publications in 2025

Klanger C, Deghmane A, **Eriksson L**, **Säll O**, **Thulin Hedberg S**, **Mölling P**, Taha M. Inactivation of the *porB* gene reduces the virulence of *Neisseria* meningitidis in transgenic mice. BMC Microbiol 2025 Aug 16;25:515. 2025:16(25:515). PMID 40818988 10.1186/s12866-025-04246-3.

Belayneh M, Alemu F, **Idosa BA**, Assefa M, Särndahl E, Abate E, **Säll O**, Gelaw B. Diagnostic comparison of microbial culture and polymerase chain reaction for the diagnosis of bacterial meningitis in a tertiary hospital, North West Ethiopia. IJID Reg. 2025 Sep 3;17:100743.

Lucidarme J, Deghmane AE, Sharma S, Meilleur C, **Eriksson L**, **Mölling P**, Claus H, van Sorge NM, Bettencourt C, Bajanca-Lavado P et al. Umrah- and travel-associated meningococcal disease due to multiple serogroup W ST-11 sub-strains pre-Hajj 2024. J Infect 2025:106558. PMID 40701332 10.1016/j.jinf.2025.106558

David Shaw, et al [**Jacobsson S** Nr. 35 **Mölling P** Nr. 57]. Quantifying the impact of the COVID-19 pandemic on invasive bacterial diseases across 27 countries and territories: prospective surveillance by the IRIS Consortium. medRxiv 2025 Jul 11, https://doi.org/10.1101/2025.07.10.25331197.

Plans for the coming Year

The culture plates used for isolating and subculturing *N. meningitidis* (GCAGP and GVCNTP) will no longer be available with CE marking under the IVDR regulation, according to the manufacturer. A decision has therefore been made to continue working either with in-house production or to replace the agar plates. This work will continue during 2026–2027.

To shorten turnaround times from the NRL, implementation of electronic results via the laboratory portal is planned for 2026.

The EUCAST laboratory has contacted the NRL to discuss the development of a disk diffusion method for antimicrobial susceptibility testing of *N. meningitidis*. The project has progressed with positive results, and the NRL has contributed well-characterized strains. The project is expected to be completed in 2026.

Work on ensuring that all European countries upload data from PubMLST to EMERT-II and EpiPulse is ongoing. The ECDC distributes a monthly surveillance report both nationally and internationally, with the aim of moving toward real-time reporting to improve international outbreak-related surveillance.

Collaboration within IBDLabNet and with ECDC will continue in 2026, including compilation of the external quality control panel distributed in 2025 for comparison of laboratory performance. Within IBDLabNet, the NRL will continue to work on assessing training needs and capacity building, providing support to countries, whole genome sequencing, and identifying areas requiring further and expanded research.

Expanded fine typing for whole genome sequencing of non-culturable isolates is planned to be established using targeted amplicon Nanopore sequencing in collaboration with the Norwegian Institute of Public Health.

Vaccination of personnel working with *Neisseria* diagnostics was initiated in 2025 and will continue during 2026.

Professional development

Continued training of existing staff in the culture laboratory is ongoing, with the aim that the entire team will be qualified for *Neisseria* diagnostics.