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# 17<sup>th</sup> EMGM Congress

# 

#### European Meningococcal and Haemophilus Disease Society

# 26-29<sup>May</sup> 2025

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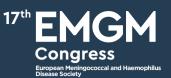




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### **SESSIONS**

Session 1: Epidemiology of IMD in the EMGM countries (Abstracts 001-008)

Session 2: Epidemiology of IMD in the EMGM countries (Abstracts 009-012)

Session 3: Strain molecular characterization (Abstracts 013-018)

Session 4: Vaccines and vaccination policies (Abstracts 019-025)

Session 5: Epidemiology of IHiD in the EMGM countries (Abstracts 026-031)

Session 6: Epidemiology of IHiD in the EMGM countries (Abstract 032)

Session 7: Outbreaks (Abstracts 033-038)

Session 8: Clinical aspects and management of IMD and IHiD (Abstracts 039-043)

Session 9: Strain molecular characterization (Abstracts 044-048)

Session 10: Thinking out of the box (Abstracts 049-051)

Session 11: Antibiotic resistance (Abstracts 051-056)



### Session 1: Epidemiology of IMD in the EMGM countries

### **001.** THE INCIDENCE AND EARLY MORTALITY OF INVASIVE MENINGOCOCCAL DISEASE (IMD) IN FINLAND

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**Introduction:** The disease burden and long-term trends of IMD in Finland in 1995-2022 were assessed in this population-based observational register study. The first results are reported here.

**Methods:** A confirmed case of IMD was defined as detection of *Neisseria meningitidis* from blood or cerebrospinal fluid (CSF) reported to the population-based laboratory surveillance system. Case-fatality proportion (CFP) was calculated as the proportion of cases resulting in death within 30 days.

**Results:** Culture-confirmed IMD cases accounted for 98% (95% confidence interval: 96-98%) of the total 948 IMD cases, of which 31% (28-34%) were identified from CSF, 48% (45-51%) from blood and the rest 21% (19-24%) from CSF and blood. The proportion of clinical manifestation of meningitis differed by age from 60% (53-67%) and 65% (59-70%) in age-groups 0-4 and 15-24 years, respectively, to 17% (12-26%) in age-group  $\geq$ 65 years.

The overall incidence per 100,000 person-years decreased from 1.14 (1.02-1.28) in 1995-1999 to 0.32 (0.26-0.40) in 2015-2019 and fell to 0.08 (0.05-0.14) during the COVID-19 pandemic. Incidence was highest among infants. Majority of all cases were caused by serogroup B (63%; 60-66%); serogroups C, Y and W accounted for 16% (13-18%), 13% (11-15%) and 3% (2-4%), respectively.

The overall CFP was 12% (10-14%): 15% (12-19%) among sepsis cases and 6% (3-9%) among meningitis cases. CFPs were highest for serogroups W (21%; 9-41%) and C (19%; 14-27%). There were no significant trends in CFP by age-group over time.

**Conclusions:** Incidence of IMD due to all serogroups has decreased since 1995. CFP has remained stable.





## **002.** LABORATORY SURVEILLANCE OF INVASIVE MENINGOCOCCAL DISEASE IN GERMANY, 2023/2024

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**Background:** In Germany, invasive meningococcal disease (IMD) must be notified to the Robert Koch-Institute, whereas meningococcal isolates and clinical samples to the German National Reference Laboratory for Meningococci and Haemophilus *influenzae* (NRZMHi) are submitted on a voluntary basis.

After the COVID-19 pandemic, the number of IMD cases started to increase at the end of 2022.

Aim: To report the epidemiology of IMD in Germany 2023/2024.

**Materials and Methods:** The data of the NRZMHi were analysed according to serogroup, genome sequencing, patients' age and antimicrobial susceptibility.

**Results:** In 2023, IMD cases reached the pre-pandemic level and further increased in 2024. MenB was predominant with comparable proportions of MenY. Only few cases were caused by MenC and MenW.

In 2023, almost all MenY isolates belonged to cc23 whereas the MenB isolates are scattered among ccs 213, 269, 32, 41/44 and 60.

Patients below 1 year and older than 60 years as well as 20–29-year-olds were most affected by IMD. MenY was less prevalent than MenB among infants and toddlers and was most prevalent in patients older than 60 years.

Most meningococcal isolates were susceptible to cefotaxime, ciprofloxacin and rifampicin, but the proportion of penicillin-resistant isolates increased. Few isolates harboured a b-lactamase or were resistant to multiple antibiotics.

**Conclusion:** After the COVID-19 pandemic, the IMD epidemiology in Germany changed significantly with an increase of MenY. Thus, the question arises whether the German immunization programme needs to be adapted.

Due to an increase of penicillin resistant meningococcal isolates ongoing surveillance is important.



## **003.** INVASIVE MENINGOCOCCAL DISEASE IN GREECE: A 2 YEAR LABORATORY SURVEILLANCE DATA (2023-2024)

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<sup>2</sup> National Public Health Organization (EODY), Athens, Greece

**Introduction:** Surveillance of Invasive Meningococcal Disease (IMD) is performed through the mandatory notification system. Clinical records are reconciled with laboratory records on national scale.

Aim: The study presents the epidemiological data for the time period 2023-2024.

**Materials and Methods:** A total of 59 IMD cases were notified in Greece for the 2 year studied period (21 and 38 cases for 2023 & 2024 respectively). Clinical samples (CSF, blood) and cultures were further identified by conventional and molecular methods.

**Results:** An increase was observed for 2023 (0.2) with further increase for 2024 (0.33) per 100 000 reaching the pre-pandemic years (average incidence 0.30 2018- 2019). An increase was observed in all age groups with an the average incidence (A.I.): 1.07 (0-4 y) 0.23 (5-14 y) 0.96 (15-24 y) and 0.07 (>24 y) per 100 000 population. A dramatic increase in incidence was observed in 2024 at the age group 15-24 y (1.46 (2024) vs 0.46 (2023) /100 000 while, a significant decrease was observed in children 0-4y 0.64 vs 1.5 for 2023 and 2024 respectively. The case fatality rates (CFR) were 5.26 (2023) and 2.8 (2024).

Among the 59 laboratory confirmed IMD cases, MenB was identified in 81.3 % (48/59) followed by MenY (10.1%; 6/59) and MenW (1.7%; 1/59). The highest average incidence rate for MenB was observed in age groups of <1 -4y (A.I. 1.07) and 15-24y (0.96 Al). The 6 MenY cases were related to the age groups <1 y (n=2), 5-15y (n=2) and >60y (n=2) all belonging to 23 cc.

The most predominant clonal complexes in both years were 213 cc and 1572 cc, and porA combinations 22-14 and 7-2,4 for VR-1, VR-2 respectively, all MenB associated. Further fhbp analysis revealed that the most predominant combination was 3.45/A05\_001.

**Conclusions:** A dramatic increase was observed during the past two years, MenB was the most predominant, while MenY and MenW cases remain low most probably due to the implementation of the MenACYW vaccination program in adolescents, since 2011.



#### **004.** INCREASE IN INVASIVE MENINGOCOCCAL DISEASE SEROGROUP B POST-PANDEMIC (2022-2024) IN ADOLESCENTS IN THE NETHERLANDS

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**Introduction:** After lifting COVID-19 measures in 2021, several European countries reported increases in Invasive Meningococcal Disease serogroup B (IMD-B) amongst adolescents. We explored temporal patterns of IMD-B incidence between the pre-COVID-19 pandemic period (2015-2019) and the period after lifting COVID-19 measures (2022-2024) in the Netherlands, where IMD-B vaccination is not implemented.

**Methods:** IMD-isolates were serogrouped by the Netherlands Reference Laboratory for Bacterial Meningitis using Ouchterlony gel-diffusion. Statistical analyses were performed using national surveillance data and population numbers from Statistics Netherlands. Quarterly incidence rate ratios (IRR) were calculated by dividing median IMD-B incidences from 2022-2024 by those from 2015-2019.

**Results:** The median IMD-B incidence was 0.45 per 100,000 (n = 67-79 annually) in 2015-2019 and 0.63 per 100,000 (n = 73-119) in 2022-2024. The highest increase from 2015-2019 to 2022-2024 occurred in the age group 15-24yrs (0.87 to 1.81 per 100,000, 108%) compared to 13% (2.97 to 3.34 per 100,000), 47% (0.37 to 0.54), and 8% (0.20 to 0.22) in < 5yrs, 5-14 yrs and 25+yrs, respectively. The IRR in 15-24yrs rose sharply from Q2 2022 to Q2 2024 and in age 5-14yrs high peaks were observed in Q1 of 2023 and 2024. The IRR among <5yrs and 25+yrs rose slightly in 2024, although numbers within groups were small.

**Discussion:** In the Netherlands, the IMD-B incidence increased after lifting COVID-19 measures. The highest increase was seen in adolescents and occurred throughout 2022-2024. Other age groups showed intermittent increases or elevated incidences at the end of the '22-'24 period.



#### 005. INVASIVE MENINGOCOCCAL DISEASE IN NORWAY, 2020-2024

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Invasive meningococcal disease (IMD) cases reported to the Norwegian Surveillance System for Infectious Diseases increased over the period 2020-2024, from 4 and 5 cases during the pandemic years to 16 and 15 cases in 2023 and 2024, respectively. The mean age of the 50 individuals diagnosed with IMD over the 5-year period was 35.6 years but decreased to 22.9 in 2024.

Forty-three isolates from these IMD patients were submitted to the National Reference Laboratory for analyses using serogroup agglutination, whole genome sequencing and antimicrobial resistance testing. Cerebrospinal samples from culture-negative cases were investigated with RT-PCR for species, serogroup and subtype identification. The most prevalent serogroups were B (46%) and Y (36%). Additionally, there were 3 cases of W, 2 cases each of serogroups A, C, and W/Y. Altogether, there were 25 sequence types, and 11 clonal complexes represented among the 43 isolates. Of these, 53% belonged to clonal complex 23, with ST-23 being the predominant sequence type. Except for two ST-192 isolates, all serogroup B isolates had unique sequence types. Two isolates were resistant to penicillin (MIC = 0.5 mg/L), while all isolates were susceptible to the other tested antibiotics.

The number of IMD cases in Norway has increased following the pandemic, with a notable rise among teenagers in 2024. Ongoing surveillance is essential for identifying trends and directing public health initiatives.







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**Introduction:** Neisseria meningitidis is a significant etiologic agent of severe diseases, particularly meningitis and septicaemia. This study aims to characterize the epidemiology of invasive meningococcal disease (IMD) in Poland, where population-based vaccination against meningococci has not yet been implemented.

**Material:** The study focused on meningococci recovered from invasive cases confirmed by the National Reference Centre for Bacterial Meningitis (NRCBM) between 2023 and 2024.

**Methods:** The investigation encompassed serotyping, antimicrobial susceptibility testing, and whole genome sequencing.

**Results:** Between 2023 and 2024, the NRCBM confirmed 193 IMD cases. In 2023, the overall incidence of IMD was 0.26/100,000, with a notably higher rate of 8.69/100,000 among patients under one year of age. Meningococci serogroup B (MenB) was responsible for the majority of infections at 69.9%, followed by serogroup C (21.5%), W (8.3%), and Y (2.6%). All strains demonstrated susceptibility to penicillin, cefotaxime, chloramphenicol, rifampicin, and ciprofloxacin.

In the analysis of sequenced meningococci, 12 clonal complexes (cc) were identified. The most common were 9316cc (35.4%), 32/ET-5cc (13.1%), and 41/44cc (12.1%). Among MenB isolates, the predominant were 9316cc (28.8%), ST-32/ET-5cc (17.8%), and 41/44cc (12.3%). For MenC isolates, ST-103cc was most frequent at 28.6%, followed by ST-41/44cc and 9316cc at 21.4% each. All MenW isolates belonged to 9316cc.

**Conclusions:** Poland has maintained a low incidence rate of IMD remaining below pre-pandemic levels. The recently established clonal complex, 9316cc, remains predominant in Poland and encompasses all serogroups. MenW cases have returned to the lower levels observed prior to 2019.





RGANIZED B

### **007.** SURVEILLANCE OF INVASIVE MENINGOCOCCAL DISEASE IN PORTUGAL FROM 2020 TO 2024

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**Introduction:** Since 2002, laboratory surveillance of Invasive Meningococcal Disease (IMD) has been carried out by the National Reference Laboratory for *Neisseria meningitidis*, at the National Institute of Health Doutor Ricardo Jorge, Portugal. This study aims to analyse the epidemiology of IMD and the genetic diversity of *Neisseria meningitidis* strains from 2020 to 2024.

**Material and Methods:** Suspected IMD cases and *N. meningitidis* isolates were sent to the reference laboratory for confirmation and strain characterization. Invasive isolates were characterized by WGS (Illumina) and sequences were submitted to the PubMLST/Neisseria database.

**Results:** Between 2020 to 2024, 125 IMD cases were confirmed. Annual incidence rate ranged from 0.36 cases/100,000 inhabitants in 2020 to 0.32 in 2023 [1, 2]. Serogroup B was the most prevalent (49.6%), followed by serogroups Y (14.4%), W (13.6%) and C (5.6%). Serogroup W mainly affected those over 45 years old (58.8%). *In silico* analysis of 89 (71.2%) isolates identified major clonal complexes (cc): B-cc213 (22%) and cc41/44 (18%), Y-cc23 (80%), W-cc11 (66.7%), and C-cc11/ cc103 (33.3% each).

**Conclusions:** Compared to previous studies (2003-2020), the incidence of IMD in Portugal has decreased [1-3]. However, serogroup B remains the leading cause of IMD, raising concerns, particularly due to cases in children and emerging clusters with low vaccination coverage (e.g. serogroup B cc213) [4]. In contrast, serogroup W cases have increased, especially among adults [2, 3]. This study highlights the importance of laboratory surveillance for understanding IMD epidemiology and monitoring long-term trends.

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#### 008. EPIDEMIOLOGY OF INVASIVE NEISSERIA MENINGITIDIS IN SLOVENIA, 2010-2024

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**Introduction:** In Slovenia, we have been actively monitoring the occurrence of invasive diseases caused by *Neisseria meningitidis, Haemophilus influenzae* and *Streptococcus pneumoniae* since 1993, as a part of a national surveillance project.

**Aim:** The objectives of our study were to characterise invasive *N. meningitidis* in Slovenia from 2010-2024.

**Materials and Methods:** Invasive *N. meningitidis* isolates from all Slovenian microbiological laboratories were collected at the Department of Public Health Microbiology in Ljubljana. Genome sequences of the isolates were determined using Illumina NextSeq 2000 and PGM Ion Torrent (Life Technologies). Raw whole genome sequences (WGS) were de novo assembled and submitted to PubMLST/Neisseria (BIGSdb) for automated annotation and analysis.

**Results:** In the period 2010 to 2024 we received 112 invasive *N. meningitidis* isolates. The most affected age group were children under 1 year, with an average incidence of 8,6/100.000 population. The average annual incidence in children (0-14 years) was 1.4/100.000 and in adults ( $\geq$ 15 years) 0.2/100.000. The most prevalent was serogroup B (76 strains; 67,9%), followed by serogroup C (n=18; 16.1%), serogroup Y (n=15; 13,4%), serogroup W (n=2; 1,8%) and serogroup Z (n=1; 0,9%). We observed four main clonal complexes; ST-41/44 complex (n=34; 30,4%), ST-23 complex (n=13; 11,6%), ST-269 complex (n=12; 10,7%) and ST-11 complex (n=11; 9,8%). In 2024 we detected a rise in serogroup Y (ST-23 complex).

**Conclusion:** In Slovenia, the invasive *N. meningitidis* is occurring endemically, with low incidence rates over the past 15 years. Ongoing laboratory molecular surveillance is essential, especially for monitoring the increase in serogroup Y cases.

References https://pubmlst.org/software/bigsdb (Accessed 10 March 2025)





### Session 2: Epidemiology of IMD in the EMGM countries

# **009.** SURVEILLANCE OF INVASIVE MENINGOCOCCAL DISEASE IN THE CZECH REPUBLIC

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**Introduction:** Invasive meningococcal disease (IMD) has a decreasing trend in the Czech Republic in the last years. Surveillance program of IMD was initiated by the National Reference Laboratory for Meningococcal Infections (NRL) in 1993 when a new hypervirulent clonal complex (cc11) of *Neisseria meningitidis* serogroup C emerged in the country.

**Material and Methods:** *N. meningitidis* isolates from IMD cases are referred to the NRL to be confirmed and characterized by serogrouping and molecular methods. The IMD surveillance data merge NRL data and infectious disease reporting data with the exclusion of duplication. The surveillance IMD data include molecular characterisation of *N. meningitidis*, are internationally and long-term comparable and are reported to international databases

**Results:** IMD morbidity in the Czech Republic has been on a downward trend in recent years, but the age-specific morbidity of children under 1 year of age has remained high for a long time. The second and third risk groups are adolescents aged 15-19 years and children aged 1-4 years. The total IMD case fatality rate over the entire surveillance period is on average 10%, but unlike the gradually decreasing morbidity, there is no decrease in the case fatality rate. Most IMD cases are caused by serogroup B, followed by serogroup C, serogroup Y and serogroup W. In 2024, the majority of cases were caused by serogroup B (80%), and the next identified serogroup C caused only 13.3% of cases.

**Conclusions:** Precise surveillance data are necessary for providing adequate recommendation for vaccination in the country.

Acknowledgement: The project "Genomic surveillance of selected infectious diseases in the Czech Republic" (Grant agreement no. 101113387 - HERA2CZ) is co-funded by the European Union.



#### 010. INVASIVE MENINGOCOCCAL DISEASE IN SWEDEN 2023-2024

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#### S. Jacobsson<sup>1,2</sup>, H. Fredlund<sup>1</sup>, O. Säll<sup>1,5</sup>, M. Sundqvist<sup>1,2</sup>, P. Mölling<sup>1,2</sup>

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<sup>5</sup> Department of Infectious Diseases, Örebro University Hospital, Örebro, Sweden

**Introduction:** Invasive meningococcal disease (IMD) is notifiable in Sweden. The reporting system comprises of mandatory clinical and laboratory notification to the Public Health Agency of Sweden.

**Material:** Clinical samples sent to the National Reference Laboratory (NRL) for *Neisseria meningitidis* (Men) in Örebro for typing and surveillance.

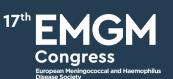
**Methods:** Antibiogram, serogrouping and whole genome sequencing were performed on isolates, whereas genogrouping and genosubtyping were performed on non-culture PCR positive samples.

**Results:** Compiled data shows 79 clinical reported cases of IMD during 2023 to 2024, of which 75 were sent to the NRL (63 culture- and 12 PCR-positive).

In 2023, 33 IMD cases were reported with incidence of 0.31 (per 100 000 population) and case fatality rate 9.1%. The group distribution was 36% MenB, 6% MenC, 27% MenY, 21% MenW and 3% MenX. Among the patients, 52% were females and 48% males with median age of 26 years (mean 38 years). Two IMD cases had an epidemiological linkage.

In 2024, 46 IMD cases were reported with incidence of 0.43, case fatality rate 4.3% and group distribution 22% MenB, 9% MenC, 57% MenY, 7% MenW and 2% MenX. The IMD cases represented 44% females and 56% males with median age of 50 years (mean 45 years) with no known epidemiological linkage.

**Conclusions:** The incidence of IMD in Sweden has almost reached the same level as before the COVID-19 pandemic. The epidemiology differs substantially between 2023 and 2024 with an increase of MenY (without clonal expansion) and higher mean age combined with lower case fatality rate in 2024.







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Introduction: The study aimed to reveal the epidemiology of MenW in Poland over the past decade.

**Material:** The study included all cases of invasive meningococcal disease (IMD) confirmed at the National Reference Centre for Bacterial Meningitis (NRCBM) between 2015 and 2024.

Methods: For all isolates, serotyping and whole genome sequencing was performed.

**Results:** Between 2015 and 2024, a total of 1,390 IMD cases were reported to the NRCBM, of which 113 (8.1%) were identified as MenW. The distribution of MenW cases changed over the years, with two significant increases noted: from 9.8% to 20.2% between 2018 and 2020 and from 7.0% to 16.6% between 2023 and 2024. Nearly half of the MenW cases occurred in children under the age of four, with a median age of 3 years. The case fatality ratio (CFR) for cases with known outcomes was 32.4% (23 out of 71 cases), and for all cases, 20.4% (23/113). Multilocus sequence typing results were available for 95 (84.1%) isolates. Among these, 17 different sequence types were identified, with 66.3% belonging to the 9316 clonal complex (CC9316) and 11.6% to CC11. During the years 2015-2021, the percentage of CC9316 ranged from 55.6 to 75.0%; however, in 2022, it decreased to 33.3%. In the following two years, 2023 and 2024, it increased again to 100% and 87.5%, respectively.

**Conclusions:** Over the past decade, a significant increase in the incidence of MenW disease in Poland has been noticed. This emphasizes the ongoing need for close monitoring of IMD.



#### 012. EPIDEMIOLOGY OF INVASIVE MENINGOCOCCAL DISEASE IN GREECE, 2004-2024

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**Introduction:** Invasive meningococcal disease (IMD) is a severe, life-threatening infection that primarily presents as meningitis or sepsis.

**Material:** The Department for VPD of the NPHO collects and analyses data for IMD cases reported through the mandatory notification system, while identification and typing is carried out by the NMRL.

**Methods:** Serogroups were determined either by slide agglutination test or by mPCR (culture negative) targeting specific capsule group genes (A, B, C, W, and Y).

**Results:** From 2004-2024, 1,170 IMD cases were reported to the NPHO, with a mean notification rate of 0.51 cases/100,000. The highest incidence was found in children aged 0-4 (mean rate: 3.95/100,000), lower in the 5-14 and 15-24 age groups (0.99 and 0.93 respectively) and did not exceed 0.20 in individuals >25 years. Most cases (93.9%) were laboratory confirmed. Among serotyped cases, (928, 79.3%), MenB was predominant (720, 77.6%) followed by MenC (41, 4.4%) and MenY (34, 3.7%) while 10.7% were non-groupable. MenB cases varied from 60.0% (2022) to 94.1% (2024) The notified incidence of serogroup B was highest in 2007 (0.60/100,000), decreased during the pandemic period (0.03/100,000), and returned to pre-pandemic levels in 2024 (0.31/100,000). Overall, 70 fatal cases were recorded [case fatality rate 6%; highest in 2018 (11.8%) and lowest in 2020-2022 (0%)].

**Conclusions:** IMD remains a public health emergency. Despite a long-term downward trend, attributed partly to the implementation of systematic vaccination, the disease returned to prepandemic levels after 2023.



### Session 3: Strain molecular characterization

#### **013.** AN IMPROVED CORE GENOME MLST SCHEME FOR NEISSERIA MENINGITIDIS

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**Introduction:** The *Neisseria meningitidis* (Nm) core genome multilocus sequence typing (cgMLST) scheme, published in 2014 and implemented on PubMLST, used 108 globally isolated genomes for its development and included 1605 loci for high-resolution comparisons. With the PubMLST database now containing 42,800 Nm genomes (as of March 2025), mostly draft assemblies, the scheme was reviewed and enhanced to maintain robust, high-resolution typing.

**Methods:** Loci were reviewed for issues encountered with draft genomes, including i) loci absent from subsets of the population, ii) loci with inconsistent start sites, and iii) loci with multiple allele assignments due to either multiple copies within the genome or paralogues.

**Results:** Problematic loci were fixed or removed, reducing the scheme to 1329 loci. Improved allele calling enabled the reduction in the allowed number of missing loci for cgST assignment from 50 to 25. Even with this stricter constraint on missing data, cgSTs could be assigned in 99.0% of all Nm assemblies of >=2Mbp total size and <=200 contigs, compared to 78.9% in the original version.

**Discussion:** Typing schemes that work for genome assemblies need to work reliably for the majority of submitted data that consists of draft genomes of variable quality. Loci removed from the new scheme were not reliably called for all assemblies and their removal allows assignment of cgSTs for more genomes. Reducing the number of allowed missing loci, which can artefactually make isolates appear more similar, increases the resolution of the scheme by improving the clustering and identification of closely related isolates.





# **014.** FLUCTUATIONS IN SEROGROUP B MENINGOCOCCAL VACCINE ANTIGENS PRIOR TO ROUTINE MENB VACCINATION IN FRANCE

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**Introduction:** Invasive meningococcal disease (IMD) of serogroup B is preventable by protein-based vaccines targeting one (Bivalent rLP2086 vaccine) or several variable proteins (4CMenB vaccine) at the bacterial surface. The 4CMenB was licensed in Europe in 2013 but has been recommended and reimbursed in France for infants over 2 months old since April 2022. The bivalent rLP2086 vaccine was licensed in Europe in 2017 for subjects of 10 years and older. Evaluating strain coverage and fluctuations prior to large scale vaccine use is highly informative.

**Material:** We whole genome sequenced 1691 cultured serogroup B invasive isolates recovered between 1975-2022 in France, using Illunmina sequencing.

**Methods:** We scored sex, and age groups of subjects. We also scored clonal complexes (CC) and the predicted coverage rates using gMATS and the MenDeVAR.

**Results:** The period was divided into four periods 1975-1986, 1987-1998-1999-2010 and 2011-2022. Our data clearly show significant differences in the distribution of alleles encoding the vaccine-covered antigens between these four periods. The clonal complex (CC) distribution also differed between the two periods with disappearance of CC8 since 2011 and drastic decreases in CC11 since 1999. MenDeVar-predicted coverage fluctuated between 46.8 and 60.6% during the four periods for the 4CMenB and between 63.4% and 81.3% for rLP2086. For 4CMenB, coverage was higher using gMATS and varied between 74.5% and 85.0%. Fluctuations were also observed for all age groups.

**Conclusions:** IMD epidemiology is continuously changing with fluctuation in vaccine strain coverage over the 48 years prior to the routine implementation of the vaccines.







## **015.** THE NASOPHARYNGEAL MICROBIOME IN RELATION TO NEISSERIA MENINGITIDIS CARRIAGE DYNAMICS

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The human pathogen *Neisseria meningitidis* may cause invasive meningococcal disease and is often carried asymptomatically in the nasopharynx. Through next generation sequencing, the microbiome has been revealed to be complex and variable. The interplay between *N. meningitidis* and other microbes in the nasopharynx has not yet been thoroughly investigated. Studying host-bacteria interactions and meningococcal carriage in relation to other species may clarify the colonization and pathogenesis of *N. meningitidis*. This study aimed to investigate changes in the nasopharyngeal microbiome in correlation to carriage status over time of *N. meningitidis*.

From a previous longitudinal carriage study among Swedish university students, 170 nasopharyngeal swab samples, including both positive and negative samples from the same individual, were selected. All samples were analyzed through metagenomic 16SrRNA sequencing using 16S Barcoding Kit 24v14 from Oxford Nanopore. The reads were analyzed through the gms-16S pipeline, https://github.com/genomic-medicine-sweden/gms\_16S.

Significant differences in relative abundance for carriage status were seen for some genera. Both Spp. *Veillonella* and *Prevotella*, displayed higher abundance in those who had gone from positive to negative carriage status, and lower in those who had become carriers of *N. meningitidis*. Inversely, spp. *Haemophilus* showed higher abundance in those who had become carriers and lower in those who went from positive to negative carriage status. No significant difference in alpha diversity between carriage status was observed.

Carriage status of *N. meningitidis* could be correlated to differences in microbial composition. Further microbiome analyses are underway, including metagenomic shotgun sequencing and investigations into correlations with risk factors for meningococcal carriage.



#### **016.** A LIFE IDENTIFICATION NUMBER (LIN) BARCODING SYSTEM FOR NEISSERIA MENINGITIDIS: ADVANCEMENT IN STABLE BACTERIAL TYPING AND HIGH-RESOLUTION OUTBREAK INVESTIGATIONS

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Accurately communicating bacterial diversity is key, not only for classification, but also for pathogen surveillance, epidemiology, and population biology. Currently, the seven loci MLST has been successful for determining *N. meningitidis* population structure, further enhanced using fine typing antigens. Life Identification Number (LIN) barcodes are a novel way of describing bacterial populations through stable hierarchical clustering and nomenclature. These are based on allelic differences between core genome Sequence Types (cgSTs), assigned from representative core genome MLST (cgMLST) profiles. *Neisseria meningitidis* cgMLST v3 (1,329 loci), available on pubMLST, was used as the foundation for this work.

A curated dataset of 6,131 *N. meningitidis* isolates, encompassing up to 200 high-quality isolates from each clonal complex (CC), were used for LIN code development. The cgSTs for each isolate were subject to creation of a pairwise distance matrix and statistical analysis using Minimum Spanning Tree-based clustering. Overall, 13 LIN thresholds were chosen to represent different genetic lineages. These have been provided human-readable nicknames that represent MLST and MLEE describers. Defined *N. meningitidis* LIN thresholds are openly accessible for use on pubMLST.

Several published outbreak datasets were used to validate the LIN codes, which illustrated highquality and fine resolution for population analysis. In addition, we were able to differentiate the Hajj and South American CC-11 isolates (n = 4,740) at the clonal group level of 5.04% (67 loci) allelic mismatches. Overall, LIN codes will be important for distinguishing between closely related strains for outbreak investigations, contributing to understanding of strain theory, and aiding vaccine development.







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**Background:** The present study investigates the molecular epidemiology of invasive *Haemophilus influenzae* (Hi) in Belgium, a subject that is currently under-described.

**Material and methods:** During the first half of 2022 and 2023, the National Reference Centre collected 139 invasive *Hi* strains. All strains were subjected to whole genome sequencing (WGS) using a NovaSeq and sequences were analysed using the BioNumerics 8.1 software.

**Results:** The most prevalent clonal complex (CC) was CC3 (15.1%), followed by CC11 (13.7%) and CC107 (7.2%).

The presence of the resistance genes blaTEM-1B, associated with ampicillin resistance, was observed in 17.3% of the strains, while a significant proportion of the strains (24.5%) exhibited mutations in the *ftsl* gene. Five of these strains belonged to the group III-like group, whose mutations are linked to high-level beta-lactam resistance. Of these five strains, three formed a cluster and belonged to CC3. The mutations responsible for isolated resistance to cefuroxime (S357N) and for cefotaxime (S385T) were identified exclusively in these five 'group III-like' strains.

The parE (fluoroquinolone resistance) and tetB (tetracycline resistance) genes, as well as an insertion of five amino acids in FoIP (cotrimoxazole resistance), were identified in 0.7%, 2.2%, and 12.2% of the strains, respectively. The WGS appears to adequately predict the phenotypic susceptibility.

**Conclusion:** In Belgium, most invasive *Hi* strains belong to CC3. Almost 25% of strains carry *ftsl* mutations and, for the first time, a cluster of highly resistant strains was documented in Limburg, highlighting the need for continuous monitoring.





# **018.** MOLECULAR CHARACTERIZATION OF NEISSERIA MENINGITIDIS STRAINS CAUSING NON-INVASIVE DISEASE IN PORTUGAL FROM 2012 TO 2024

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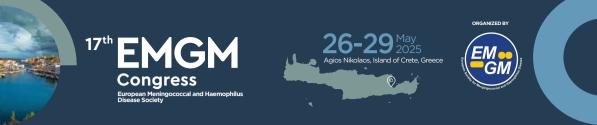
**Introduction:** Non-invasive meningococcal disease (NIMD) is not notifiable, and the prevalence of serogroups and antimicrobial resistance (AMR) are unknown. This study aims to investigate the genetic diversity of non-invasive isolates identified in Portugal (2012-2024), assess their genomic relationships with Portuguese invasive isolates and identify AMR profiles.

**Material and Methods:** All non-invasive *N. meningitidis* isolates were characterized by whole genome sequencing and the sequences submitted to the PubMLST/Neisseria.database. For antimicrobial susceptibility testing, antibiotic gradient strip diffusion (Etest) was used.

**Results:** A total of 141 non-invasive isolates were characterized by WGS with 88% identified from respiratory secretions. Serogroup B was the most prevalent (40.4%), followed by serogroups Y (10.6%), C and E (3.5% each), W, X and Z (1.4% each). Capsule null (*cnl*) isolates accounted 33.3%. *In silico* analysis revealed the main clonal complexes (cc): B-cc41/44 (21%) and cc162 (14%), Y-cc23 and cc103 (33.3% each) and *cnl*-cc53 (38.3%). Isolates belonging to cc11 were predominantly serogroup C (40%) and only 1 isolate was identified as serogroup W. All isolates were sensitive to ceftriaxone and 67.9% of the isolates were penicillin-nonsusceptible, while 2.9% and 3.9% were resistant to ciprofloxacin and rifampicin, respectively.

**Conclusions:** In this study, we identified non-invasive populations with similar genetic diversity when compared to invasive populations in previous studies[1]. In contrast, NIM isolates showed increased levels of resistance to penicillin and several isolates showed resistance to antibiotics used in IMD prophylaxis. These results emphasise the need for more studies on AMR among meningococci in order to ensure the effective use of antibiotics in the treatment of meningococcal disease.

References: 1- Bettencourt, C., Nunes, A., Nogueira, P., Duarte, S., Silva, C., Gomes, J. P., & Simões, M. J. (2023). Epidemiology and genetic diversity of invasive Neisseria meningitidis strains circulating in Portugal from 2003 to 2020. International Microbiology. https://doi.org/10.1007/s10123-023-00463-w



### **Session 4: Vaccines and vaccination policies**

# **019.** CENTRE OF RESEARCH EXCELLENCE IN NEISSERIA DISEASE CONTROL (NEIS CRE): PROTECTION AGAINST MENINGOCOCCAL DISEASE AND GONORRHOEA WITH ONE VACCINE

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**Background:** The Centre of Research Excellence in Neisseria disease control (NEIS CRE) aims to determine the most effective immunisation program for prevention of invasive meningococcal disease (IMD) and gonorrhoea globally, using one vaccine (4CMenB). Four research themes will address this aim: 1. Duration of protection; 2. Program safety; 3. Enhancing vaccine uptake; 4. Cost effectiveness.

**Methods:** A triangulation approach, using case-control and cohort studies in South Australia (SA) and Northern Territory (NT), Australia. Vaccine effectiveness (VE) estimates against IMD used controls from the Australian Immunisation Register; VE against gonorrhoea used Chlamydia controls. Vaccine Impact was estimated as adjusted incidence-rate-ratios (aIRR) in pre-vs-post-program implementation years using negative binomial regression.

**Results:** For IMD in SA, VE=98.5% (95%CI 81.9-99.9%;p=0.001) for three-doses and VE=64.2% (95%CI 7.4%-86.1%;p=0.034) for two-doses in infants. In adolescents, two-dose VE=92.3% (95%CI 34.3%-99.1%;p=0.019). There was a 72.8% relative reduction in IMD B disease in infants <12 months old (aIRR=0.273 (95%CI 0.120%-0.622%;p=0.002) and 76.2% reduction in adolescents aged 15-18 years (aIRR=0.238 (95%CI 0.097%-0.584%;p=0.002).

VE against gonorrhoea in adolescents in SA was 40.1% (95%Cl 31.4%-46.0%;p<0.001). VE=-6.3% (95%Cl -44.5-21.8) >60 months post-vaccination compared to those 3-60 months post vaccination (VE=41.8% (95%Cl 34.0%-48.7%)). The risk of a second gonococcal notification was lower in vaccinated gonococcal cases (adjusted Hazard Ratio (aHR)=0.709 (95%Cl 0.524-0.960;p=0.026)). In the NT, VE=34% (aHR 0.656 (95%Cl 0.477–0.902);p=0.009) against gonorrhoea.

**Conclusions:** 4CMenB demonstrates high effectiveness against IMD and moderate effectiveness against gonorrhoea up to five years post-vaccination and offers benefit to high-risk groups for both diseases. Waning effectiveness was observed for gonorrhoea at 5 years.



#### **020.** REDUCED INTERVAL MENINGOCOCCAL B VACCINATION IN UK INFANTS FOR EARLIER PROTECTION AGAINST DISEASE: A RANDOMISED COMPARISON OF PRIMARY IMMUNISATION SCHEDULES

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**Background:** The group B meningococcal vaccine (4CMenB) is given to infants in the UK with an 8-week interval (at 8 and 16 weeks) with a booster at 1 year. A shorter-interval primary immunisation schedule could address the incidence peak of meningococcal cases now seen in younger infants.

**Methods:** This randomised controlled trial in term infants compared the standard 8+16-week schedule with a shorter-interval 8+12-week schedule; the 13-valent pneumococcal conjugate vaccine (PCV13) moved from 12 to 16 weeks, to accommodate. Meningococcal hSBA and serotype-specific pneumococcal antibodies were tested at one-month post-primary, pre-booster, and one-month post-booster. Safety diaries were completed for 7-days after each vaccination.

**Results:** 221 infants were randomised across 6 sites. A shorter-interval schedule had no effect on proportions of infants achieving protective hSBA titres ( $\geq$ 4) against 3/3 tested strains (p>0.05); almost all infants were putatively protected in both groups.

Although post-primary hSBA GMTs were lower against 3/3 tested strains in the shorter-interval group, pre-booster GMTs were similar, and post-booster GMTs were higher, although only significantly for NZ98/254 (p=0.005).

For serotype-specific pneumococcal responses, PCV13 at 16 vs. 12 weeks led to significantly higher pre-booster GMCs for 10/12 serotypes and higher proportions achieving protective thresholds (≥0.35µg/mL) for 4 serotypes. Post-booster responses were equivalent between groups.

Both schedules had similar safety profiles, however diary data demonstrated significantly more prevalent irritability and crying with the standard 8+16-week 4CMenB schedule.

**Conclusions:** A shorter-interval 4CMenB schedule is less reactogenic and could further reduce cases in infants without compromising the infant pneumococcal immunisation programme.

Disclosure of funding:

This study was supported by GSK Supported Studies Programme Protocol 213329.



# **021.** 4CMenB COVERAGE OF SEROGROUP B MENINGOCOCCI - ENGLAND - 2015 TO 2023

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**Introduction:** In September 2015, the UK became the first country to implement 4CMenB into the national infant immunization program at a reduced 8 week, 16 week and 1 year schedule. This study presents 4CMenB antigen genotyping and MATS coverage data for all English invasive MenB isolates from vaccine eligible cohorts from 2015 to 2023.

**Methods:** Vaccine coverage of all invasive MenB isolates from 2015 to 2023 was analysed using the Meningococcal Antigen Typing System (MATS). Genotyping utilised the MRF Meningococcus Genome Library.

**Results:** Among all ages, the MenB clonal complex and sequence typing distribution distribution was stable over the 8 years studied. Among vaccine eligibles, about 96% of MenB cases were among  $\leq$  3 years olds. There were >80% fewer cases in the second year of life, compared to the first. Two thirds of MenB isolates were MATS positive for at least one antigen among zero to two-dose vaccinees. Among three-dose vaccinees, the proportion of non-covered strains decreased with patient age was observed.

**Conclusions:** 4CMenB has reduced MenB disease in the vaccine cohort over the study period. However, many strains from fully vaccinated cases were MATS positive, which may indicate, for example, a lack of response to the vaccine or antibody waning.





# **022.** IMPACT OF AN IRREGULAR INTRODUCTION OF THE 4CMENB VACCINE ON THE CHILDHOOD VACCINATION SCHEDULE IN SPAIN

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**Introduction:** The 4CMenB vaccine has had an irregular implementationh in Spain, first privately in pediatrics since 2015, with high coverage rates, being included (free of charge) in 4 regional calendars between 2019 and 2022. Finally, the vaccine was introduced into the vaccination schedule throughout Spain in 2023. Because the irregular introduction, together with the pandemic period, it is difficult to determine the impact of the vaccine's introduction. We will attempt to address this question by analyzing strains/clinical samples in vaccinated children between 6 months to 2 years of age.

**Methods:** The Spanish National Reference Laboratory for Meningococci receive around 80% of the confirmed cases all around the country. All the strains/ clinical samples received between 2016 and 2024 were grouped, and molecular characterized by whole genome sequence.

**Results:** The results correspond to 912 MenB strains and clinical samples received during the period analyzed. While strains from children between 6 months and 1 year of age accounted for 26% of serogroup B cases in 2016, they only represented 6% in 2024 (31 cases compared to just 9). In 2024, only 1/8 isolate was potentially covered by the vaccine, compared to 8/21 in 2016.

**Discussion:** The 4CMenB vaccine has had a delayed impact over time while being administered in private practice, with significant coverage rates, until it was finally introduced into the vaccination schedule (free of charge) in 2023, and it is then that the impact becomes most evident.





# **023.** MULTI-COMPONENT VACCINE CANDIDATES AGAINST NON-TYPEABLE HAEMOPHILUS INFLUENZAE

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**Background:** Haemophilus influenzae (Hi) is a Gram-negative bacterium commonly found on mucosal surfaces, particularly in the respiratory tract. It can cause both local and invasive infections. The burden of infections by non-typeable *H. influenzae* (NTHi) has increased following the introduction of the *H. influenzae* type b (Hib) vaccine. The absence of a preventive strategy and rising antibiotic resistance make NTHi a growing public health concern. This study explores potential vaccine candidates against NTHi.

**Methods:** We analyzed 1,144 Hi genomes collected between 2017–2022 and identified 514 conserved genes, selecting 13 encoding membrane proteins. Among these, we focused on *Haem1295* (outer membrane protein P5, OMP5) and *Haem1040* (outer membrane protein 26, OMP26), OMP5 binds human complement regulatory protein factor H (FH), while OMP26 enhances immune responses. The genes encoding these proteins were cloned, overexpressed, purified, and tested in active and passive protection models using systemic infection in mice. Additionally, we analyzed the effect of anti-OMP5 antibodies on FH binding and C3b/C5C9 deposition using flow cytometry.

**Results:** OMP5 and OMP26 were immunogenic in human infections. Vaccination conferred protection against both homologous and heterologous NTHi strains in mice. Anti-OMP5 antibodies enhanced C3b and C5C9 deposition, promoting bacterial clearance through opsonophagocytosis and lysis.

**Conclusion:** Our results highlight that, the conserved immunogenic and surface-exposed proteins (OMP5 and OMP26) in NTHi are appropriate vaccine candidates against NTHi isolates with an additional benefit to vaccinate using proteins that is involved in bacterial virulence.



#### 024. SEROGROUP Y INVASIVE MENINGOCOCCAL DISEASE IN A CONSCRIPT PREVIOUSLY VACCINATED WITH MENINGOCOCCAL ACWY CONJUGATE VACCINE

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**Introduction:** Meningococcal ACWY vaccination has been offered in Finland to all new conscripts starting compulsory service since 1982. We describe a case of serogroup Y invasive meningococcal disease (IMD) in a previously vaccinated conscript.

**Results:** In January 2025, serogroup Y IMD was diagnosed in a previously vaccinated 19-year-old conscript who had started military service twenty days earlier.

The conscript developed symptoms of acute infection 15 days after MenACWY vaccination. Four days later, he was admitted to the hospital emergency department and diagnosed with IMD based on clinical signs and detection of meningococcal DNA in cerebrospinal fluid. The patient was found co-infected with coronavirus OC43. Blood culture became positive for *Neisseria meningitidis* later. The isolate belonged to serogroup Y (Y:P1.5-2,10-1:F4-1:ST-new). It was genetically related to ST-6800 (cc:23) isolates recovered from IMD and conjunctivitis patients in Finland since 2017, but differed from other cc:23 isolates in the PubMLST database.

After treatment with ceftriaxone the patient recovered. The patient had no known underlying medical conditions or medications that might increase susceptibility to IMD. Control measures were initiated immediately after IMD diagnosis. No new cases were detected.

**Conclusions:** No previously well-defined risk factors that could have predisposed the vaccinated conscript to IMD were identified. The short time between vaccination and onset of symptoms suggests that exposure to *N. meningitidis* and mucosal colonisation may have occurred before the development of a sufficient antibody response. Simultaneous infection with coronavirus OC43 may have weakened the innate and adaptive immune response, which may have exposed the patient to invasive infection.







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**Introduction:** Invasive meningococcal disease (IMD) has a decreasing trend in the Czech Republic, therefore the need for individual protection of persons at increased risk of IMD is emphasized.

**Material and Methods:** In the Czech Republic, an IMD surveillance system has been in place since 1993 and the data serve as a basis for vaccination strategy.

**Results:** The Czech Republic is one of the countries where IMD vaccination is covered by health insurance. Since 1 January 2018, vaccination against IMD has been covered for insured persons with selected medical indications. From 1 May 2020, vaccination of young children with MenB vaccine and conjugated tetravaccine ACWY has been included among vaccinations covered by health insurance and from 1 January 2022 vaccination of adolescents as well. The theoretical MenB vaccine coverage of *Neisseria meningitidis* B Czech isolates from IMD using the MenDeVAR index is sufficient. However, as new data from experimental studies are still required to determine the MenDeVAR index in PubMLST database vaccine antigens, there is an increasing proportion of isolates for which insufficient data are available and, as a result, the theoretical coverage of MenB isolates by vaccines may be underestimated. It is desirable to discuss the possibilities of updating the data for the MenDeVar index.

**Conclusions:** The fact that MenB vaccine and conjugate vaccine ACWY started to be covered by health insurance for young children and adolescents appears to play a role in the persistent decline of IMD in the Czech Republic.

Acknowledgement: The project "Genomic surveillance of selected infectious diseases in the Czech Republic" (Grant agreement no. 101113387 - HERA2CZ) is co-funded by the European Union.



### Session 5: Epidemiology of IHiD in the EMGM countries

# **026.** HAEMOPHILUS INFLUENZAE MENINGITIS IN GREECE: 12 YEAR OF CONTINUOUS SURVEILLANCE (2013-2024)

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**Introduction:** Due to mass vaccination programs implemented in all European countries, the incidence of meningitis due to Hib remains low. However, concern exists for the long-term effectiveness and possible disease replacement by other *H. influenzae* serotypes.

**Materials & methods:** All *H. influenzae* meningitis cases notified and confirmed either by culture or PCR during a 12-year period (2013-2024) were included. PCR assays were employed for the identification of *H. influenzae* (hel gene) and Hib and capsule detection (bexA gene), and further identification of serotypes a, c, d, e, f.

**Results:** Of 101 *H. influenzae* cases the majority (86%) were confirmed. A predominance of nontypeable (NTHi) was evident throughout the study period. Twelve cases were caused by Hib, while 89 cases were caused by non-b *H. influenzae* (average incidence 0.008 and 0.072/ 100.000) respectively). Serotypes f and a were identified in 3 and 1 cases respectively, while the remaining were NTHi. The few Hib cases identified were almost the same for children (<15 yo) and adults (>40 yo). The majority of NTHi (69.1%) were recorded in adults >30 y.o, while 29.6% pertained to children up to 14 y.o. It is noteworthy that 24.7% of NTHi cases were recorded in children 0-4 y.o.

**Conclusions:** Despite the reduction of Hib disease, the predominance of NTHi cases, highlights the need for constant awareness and closer surveillance of *H. influenzae* infections. Molecular techniques play an important role in the diagnosis and typing of culture-negative cases, allowing better epidemiological monitoring.



#### 027. HAEMOPHILUS INFLUENZAE MENINGITIS IN GREECE

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**Introduction:** Meningitis due to *H. influenzae* type b (Hib) remains low in Greece, although there is concern that Hib could be replaced by other serotypes or Non-typable *H. influenzae* (NTHi) especially during the post COVID-19 era (2022-24).

**Aim:** The study aims a 2 year surveillance of the disease in Greece during the post COVID-19 era and the comparison with pre- and during COVID-19 periods.

**Materials/Methods:** All cases were confirmed by culture and/or PCR. Further identification included the presence of capsule and the respective serotype.

**Results:** A total of 31 cases were reported in Greece between 2022 and 2024. Although the incidence remained low during 2020-2021 (averaging 0.02/100 000), an increase was observed during the post COVID-19 era even though there was a decrease in 2024 (0.04/100 000). Specifically, of the 31 cases one was identified as Hib (3,2%), while the rest as NTHi (30/31 – 96.8%). Among those, 5 cases (16.6%) belonged to age group 0-9 y.o and 25 (83.4%) belonged to age group over 30 y.o. A significant NT i increase was observed during the post COVID-19 era (n=30) in comparison to previous years (2020-2021, n=4) and 2018-2019 (n=14). In contrast, Hib cases remained stable (2018 (n=1) and 2023 (n=1)). Interestingly, both Hib cases were found at the age group 51-60 y.o.

**Conclusions:** Despite the significant decrease in *H. influenzae* incidence during the pandemic period, a significant increase was observed during the post COVID-19 period to even higher levels than the pre-pandemic period. Therefore, continuous surveillance is essential.



#### **028.** EPIDEMIOLOGY AND GENETIC CHARACTERIZATION OF INVASIVE HAEMOPHILUS INFLUENZAE IN PORTUGAL (2023-2024): EVOLUTION OF SEROTYPES AND ANTIMICROBIAL RESISTANCE MECHANISMS

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**Introduction and Aim:** The National Reference Laboratory for *Haemophilus influenzae* has conducted continuous surveillance of *H. influenzae* invasive disease in Portugal since 1989. Following Hib vaccine introduction in 2000, the epidemiology of the disease shifted significantly, with Hia emerging as a major concern. Our aim is to characterize invasive isolates from 2023-2024 and compare results with previous data[1-3].

Materials and Methods: A total of 152 invasive isolates, mostly from blood cultures (94.1%), were analysed using whole-genome sequencing (Illumina technology): 63.8% were male, with 21% aged ≤5 years and 51.3% aged >65 years. Phenotypic antimicrobial susceptibility was determined by microdilution following EUCAST guidelines[4].

**Results:** Nontypeable *H. influenzae* (NTHi) accounted for 78.3% of cases. Encapsulated isolates (21.7%) were distributed as follows: Hia-9.9%, Hib-7.2%, Hie-3.3%, Hif-1.3%.  $\beta$ -lactamases (TEM-1B; TEM-1A, TEM-36) were characterized in 13.8% of isolates. Resistance rates were: ampicillin-14.6%, trimethoprim-sulfametosaxol-19.2%, cefepime-3.1%, ciprofloxacin-1.5%. *In silico* MLST showed high genetic diversity among 119 NTHi isolates, with 70 STs (58.8%). ST-103 (ST-11 complex) was the most common with seven isolates, all gBLPAR. Encapsulated isolates were mostly clonal within each serotype.

**Discussion and Conclusion:** Compared to 2019-2022, invasive disease remains predominantly caused by NTHi, increasing from 65.5% to 78.3%. Hia continues to be the most frequent serotype among encapsulated isolates, though its prevalence decreased from 11.7% to 9.9%. A new ST (ST-2919) was identified in Hib. Among the six newly unassigned STs, three belong to serotype e. Notably, we observed a concerning increase in resistance, with gBLNAR prevalence rising from 14.6% to 20.3%. Ongoing surveillance is crucial to track emerging trends and guide effective public health responses.

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## **029.** EPIDEMIOLOGY OF INVASIVE HAEMOPHILUS INFLUENZAE DISEASE IN POLAND, 2018-2023

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**Introduction:** *Haemophilus influenzae* (Hinf) is a human-specific Gram negative bacterium responsible for respiratory tract infections, sepsis and meningitis. The study aimed to investigate invasive Hinf infections in Poland from 2018 to 2023.

**Materials and Methods:** Hinf strains were isolated from patients with invasive disease. Sample data were obtained from the Polish laboratory surveillance system. Susceptibility testing was performed for all isolates and whole genome sequencing (WGS) analysis for capsulated isolates only.

**Results:** Between 2018 and 2023, the NRCBM confirmed 400 Hinf invasive cases. The outcome was known for 258 cases (64.5%) and of them the case fatality ratio (CFR) was 40.3%. Most strains of Hinf were isolated from blood (90.8%). Male patients accounted for 52.3%. Forty five percent of cases were over 65 years old (n=180). Non-typeable Hinf (NTHi) strains were responsible for most invasive disease in all-age group and accounted 85.5% (342/400) of all cases. Of the 400 Hinf 16.0%, 1.0%, 4.5% were resistant to ampicillin, cefotaxime meropenem, respectively. Capsulated isolates constituted 14.5% (58/400); among them the most common serotype was type f (Hif; 63.8%), followed by serotypes: e (Hie;19.0%), b (Hib; 13.8%), and d (Hid; 3.5%). Of the 65 cases among children (<5years old), 55 (84.6%) were caused by NTHi and the remaining by Hib, Hie, and Hif. Hif, Hie and Hib isolates belonged to ST-124cc, ST-18cc and ST-6cc, respectively.

**Conclusion:** In Poland as in other countries, NTHi predominated among invasive cases across all age groups,. Capsulated isolates were clonal and distributed in a few STs.



## **030.** HIB INCREASE IN <5 YEAR OLDS DURING COVID YEARS IN THE NETHERLANDS: NO IMPACT OF VACCINE SWITCH AND RETURNING TO NORMAL

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**Introduction:** The number of invasive *Haemophilus influenzae* serotype b disease (Hib) cases in children <5 years increased during the COVID pandemic (2020-2022), with unknown cause. In 2019 and 2020, the product (DT3aP-HBV-IPV/Hib→DT5aP-HBV-IPV-Hib) and schedule (2,3,4,11→3,5,11 months) changed in the Dutch national immunisation programme (NIP), respectively. We describe trends in Hib incidence for 2015-2024 and estimated product-specific vaccine effectiveness (VE) in the Netherlands.

**Methods:** We obtained national surveillance data through obligatory notification and voluntary isolate submission to the Netherlands Reference Laboratory for Bacterial Meningitis. We serotyped isolates using agglutination with in-house sera. We determined incidences with population numbers from Statistics Netherlands. We estimated product-specific VE through a matched case-control study, with 10 controls per case (2005-2023; N=3086). Using conditional logistic regression, we estimated the odds ratio (OR) and VE was 1-OR.

**Results:** The Hib incidence in <5 year-olds ranged from 3.0-3.7/100,000 (n=26-32) in COVID-years. In 2023, the incidence was still 3.2/100,000 but decreased to 1.7/100,000 (n=15) in 2024, resembling the median incidence in 2015-2019. The VE of DT3aP-HBV-IPV/Hib and DT5aP-HBV-IPV-Hib in the year after the booster dose was 99% (95%CI 96-100%) and 100% (95%CI 97-100%), respectively. VE remained above 87% with no significant differences between products, 1-3 years post-booster.

**Conclusion:** After an unexplained increase during COVID-years, the Hib incidence in <5 year-olds returned to baseline. The VE against invasive Hib disease was high for both hexavalent vaccines. It is unlikely that changes in vaccine product caused the increased Hib incidence during COVID-years in the Netherlands.





### **031.** TRENDS IN INVASIVE HAEMOPHILUS INFLUENZAE DISEASE IN ENGLAND, 2013/14-2023/24

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**Introduction:** *Haemophilus influenzae* serotype b (Hib) vaccine was introduced in 1992. This caused a substantial decrease in the burden of Hib and, therefore, total *H. influenzae* infections.

**Methods:** The UKHSA conducts enhanced national surveillance of *H. influenzae* for England. *H. influenzae* cultures from sterile sites are routinely submitted to the UKHSA national reference laboratory for confirmation and serotyping. Confirmed cases are routinely followed-up with their general practitioners for additional demographic, epidemiological and clinical information. Here, we describe trends in overall and serotype-specific *H. influenzae* disease in England during 2013/14-2023/24 epidemiological years.

**Results:** Invasive *H. influenzae* disease decreased during COVID-19 and increased thereafter. Both encapsulated and non-encapsulated strains showed this trend, with non-encapsulated strains making up 74-87% of cases annually. In 2023/24, there were 846 laboratory-confirmed cases of invasive *H. influenzae* disease. 703 isolates were serotyped, 598 (85.1%, 10.4/million) were non-encapsulated, 17 (2.4%, 0.29/million) serotype a, 19 (2.7%, 0.33/million) serotype b, 0 serotype c, 0 serotype d, 13 (1.8%, 0.23/million) serotype e and 56 (8.0%, 0.97/million) serotype f. In 2023/24, there were 3 Hib cases in children aged <15 years, 4 in 15-44 year-olds, 7 in 45-64 year-olds and 5 in 65+ year-olds. Hia cases started increasing in 2015/16 and, following a small decline during COVID-19, have continued to increase, especially in children and older adults.

**Conclusions:** Invasive *H. influenzae* incidence is now similar to pre-pandemic levels. Hib cases remain controlled because of the well-established national immunisation programme, but the ongoing increase in Hia disease will require careful monitoring.



### Session 6: Epidemiology of IHiD in the EMGM countries

#### **032.** INVASIVE BACTERIAL DISEASE SURVEILLANCE ENHANCEMENT IN THE MIDDLE EAST AND NORTH AFRICA (MENA): MENINGITIS AND SEPTICEMIA MAPPING NETWORK (MenMap)

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**Background:** Vaccine-preventable invasive bacterial diseases (IBD) pose a significant public health burden across the MENA region. Recognizing critical gaps in IBD surveillance and laboratory diagnostic capacity, the Meningitis and Septicemia Mapping Network (MenMap) was established to enhance regional collaboration, strengthen laboratory capacity, and improve epidemiological surveillance in Jordan, Egypt, and Iraq.

**Objectives:** MenMap aims to determine the contribution of *Neisseria meningitidis, Streptococcus pneumoniae*, and *Haemophilus influenzae* to invasive bacterial meningitis and/or septicemia, by implementing real-time PCR diagnostics, and improving laboratory capacity in the region.

**Methods:** Sentinel surveillance was implemented in 16 hospitals, targeting children aged 1 month to 18 years. Standardized protocols included clinical evaluations and real-time PCR for pathogen identification. Training programs were conducted, and online dashboards were developed to support data visualisation. An External Quality Assessment programme ensured laboratory diagnostic accuracy.

**Results:** Between December 2023 and November 2024, 2,104 suspected cases were reported, with 191 (9%) confirmed. *S. pneumoniae* was the most prevalent pathogen (90.0%), followed by *H. influenzae* (7.9%) and *N. meningitidis* (2.1%). *H. influenzae* cases were identified as type b, while among the four *N. meningitidis* cases, two were serogroup A, one was serogroup B, and one was undetermined. Confirmed cases were primarily reported in Iraq (63.3%), while nearly 62% across the three countries occurred in children under five years of age.

**Conclusion:** MenMap contributes to strengthening bacterial meningitis surveillance in the MENA region, with ongoing efforts to improve pathogen characterization and public health decisions.

#### **Conflict-of-Interest Declaration**

The current study is funded by Sanofi.

Magid Al-Gunaid, Tareq Al-Sanouri, Sara Abu Khudair, Zeina AbdelMajeed, Deema Bakri, and Lamia Al-Kershi are employed by GHD EMPHNET, an organization that conducts epidemiological studies on infectious and non-infectious diseases, including those funded by Sanofi and other organizations, outside the scope of this work.

Muhamed-Kheir Taha performs contract work for the Institut Pasteur funded by GSK, Pfizer, and Sanofi and holds a patent (NZ630133A) with GSK titled "Vaccines for Serogroup X Meningococcus." Ray Borrow conducts contract research on behalf of UKHSA for GSK, PATH, Pfizer, and Sanofi. Dominique A. Caugant and Saber Yezli have no conflicts of interest related to this project. Amine Amiche, Florence Coste, and Alp G. Dogu are employees of Sanofi.



### **Session 7: Outbreaks**

### **033.** UNIVERSITY BASED OUTBREAK OF INVASIVE MENINGOCOCCAL DISEASE IN GREECE, JANUARY-MARCH 2024

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Introduction: Outbreaks of Invasive Meningococcal disease (IMD) among university students are extremely rare in Greece.

**Material:** The NPHO's VPD Department analyses data for IMD cases and outbreaks, reported through the mandatory notification system, while identification and typing is carried out by the NMRL.

**Methods:** Serogroups were determined either by slide agglutination test or by mPCR (culture negative) targeting specific capsule group genes (A,B,C,W, and Y). Further molecular analysis included PorA, fhbp, MLST, and WGS (in culture positive samples).

**Results:** From 11 January- 6 March 2024 three IMD cases in university students aged 18-20 in Patras were reported to the NPHO. These cases met the criteria for an outbreak in a university setting (three associated cases within a three-month period). Genotypic analysis for PorA, and MLST respectively, revealed the following characteristics in 2/3 cases: B:7,16,35, 32cc (ST-32) and B: 7-12,14,35-1, 1572cc (ST1572) (third case). Further analysis on vaccine antigens by MenDeVaR index revealed in two cases exact match and cross-reaction for 4CMenB and MenB-FHbp respectively, while in the third one there were insufficient data although it belonged to fhbp type A05\_001 Subfamily A. In response, the NPHO undertook several measures including enhanced case detection, providing chemoprophylaxis, and administering targeted MenB vaccination to close contacts. Following the comprehensive implementation of these measures, no additional cases were reported.

**Conclusions:** Despite the low overall incidence of IMD in Greece, university students face a heightened risk of IMD caused by MenB, and potential outbreaks. Key factors contributing to the avoidance of new cases during outbreaks include enhanced detection and reporting, administration of chemoprophylaxis, use of available tools for molecular identification availability of MenB vaccines, and increased awareness among students.







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**Introduction:** We are describing a cluster of four IMD young adults cases associated with a serogroup B strain. The outbreak was initially associated with attendance at a bachelor party but also a holiday trip. Cases 1 and 4 died, giving a very high mortality rate of 50%. Cases. The aim of this report is to analyse the characteristics of this outbreak, including a molecular analysis of the isolates.

**Methods:** For the cases 1 and 4 an isolate was available from blood sample; the cases 2 and 3, were only confirmed by PCR from CSF. Molecular characterization (including PorA, FetA, MLST and fHbp genotyping) for all 4 cases (the 2 N. meningitidis isolates and the 2 non-cultured confirmed cases) was carried out. A genomic comparison of strains belonging to the same cc to which the outbreak strain wase associated was also performed.

**Results:** Both the isolates and clinical samples were sero/genogroup B ST-32 clonal complex, with a genosubtype VR1 19-54, VR2 15, not previously. Potential coverage of the outbreak strain by any of the MenB available vaccines (4CMenB and rLP2086) could not be predicted by molecular tools, so bactericidal response by 4CMenB vaccine against outbreak strain was measured by human serum bactericidal antibody assay (hSBA), definig the outbreak strain as covered by the vaccine.

**Discussion:** Genomic investigation showed the acquisition of this new VR1 variant 19-54 has occurred in a small group of isolates from clonal complex 32, and at least currently, it appears to be limited to that small group. The evolution of these strains with VR1 19-54 will have to be closely monitored, as might confers a greater transmission capacity.



#### **035.** OUTBREAK OF INVASIVE HAEMOPHILUS INFLUENZAE SEROTYPE B (HIB) INFECTIONS IN GERMANY AMONG PERSONS EXPERIENCING HOMELESSNESS AND DRUG ABUSE

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**Introduction:** Since the introduction of the *Haemophilus influenzae* serotype b (Hib) vaccination invasive Hi infections are rare and usually sporadic in Germany.

We report an ongoing Hib outbreak among adults persons experiencing homelessness in Hamburg. To our knowledge, a similar outbreak has only been reported once.

**Methods:** All invasive Hi isolates are serotyped by slide agglutination and PCR. Results are reported to the submitting laboratory and the local health authorities. Disease clusters identified through spatio-temporal proximity are also notified. Genome sequencing was done of all presumed outbreak isolates.

**Results:** Increase of Hib cases 11/2024-01/2025 in Germany lead to spatio-temporal detection of three cases in Hamburg two weeks apart. Local health authorities investigated that all cases were using facilities for the homeless and showed drug abuse. Presently, six invasive Hib infections from Hamburg and two from Mecklenburg-Western Pomerania were linked to the outbreak, three patients died.

Adhoc carriage investigation in a homeless shelter showed no additional Hib carriage in 47 residents of the shelter. Genome analysis revealed that all six Hib outbreak isolates differed in <6 alleles in the PubMLST cgMLST scheme. Phylogenetic comparison showed that the outbreak strains differ from other circulating strains in Europe. Further results will be reported as the outbreak is ongoing.

**Conclusions:** This event highlights the outbreak potential of Hib even in the post-vaccine era and emphasizes the importance of ongoing surveillance. Spatio-temporal analysis of infections and genome analysis are valuable epidemiological tools for investigating disease spread and aiding in the decision-making process for containment measures.



#### **036.** ABILITY OF MENB-FHBP-CONTAINING VACCINES TO PROVIDE IMMUNE PROTECTION AGAINST SEROGROUP B SEQUENCE TYPE 1161 UK UNIVERSITY OUTBREAK STRAINS

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**Introduction:** Post-COVID-19-lockdown resurgences of meningococcal serogroup B (MenB) disease among older adolescents/young adults began in England in 2021 and included a university outbreak in southwest England. One strain caused ≥5 outbreak cases and potentially 6 others, some from other English regions. We assessed potential coverage of outbreak-associated isolates by MenB vaccines (4CMenB, MenB-fHbp, MenB-fHbp containing MenABCWY).

**Methods:** Core genome analyses of outbreak-associated and closely-related isolates were performed using PubMLST.org Genome Comparator. For 3 outbreak isolates, fHbp expression was quantified using flow cytometric meningococcal antigen surface expression (MEASURE) assay. Isolate susceptibility to MenB-fHbp induced antibodies was evaluated in hSBA assays using paired prevaccination and postvaccination serum samples from 10–25-year-olds who received 0-,6-month MenB-fHbp or MenABCWY schedules. 4CMenB isolate coverage was predicted using genetic meningococcal antigen typing system (gMATS) and Meningococcal Deduced Vaccine Antigen Reactivity (MenDeVAR) index.

**Results:** All 3 isolates belonged to ST-1161 clustering in 1 monophyletic group. One isolate harbored an fHbp peptide variant (B24/peptide1) different from others (B09/peptide13). fHbp-expression levels across isolates were >1000 MEASURE mean fluorescent units (threshold for likely MenB-fHbp induced antibody susceptibility). hSBA seroprotection (titers ≥1:8) and seroresponse (≥4-fold rise from baseline) rates and GMTs indicated robust immune responses against all isolates among MenB-fHbp containing vaccine recipients. For 4CMenB, only fHbp was predicted by gMATS/ MenDeVAR to induce cross-protective antibodies, with prediction limited to B24-harboring isolate; B09-harboring isolate coverage was unpredictable/subject to insufficient data.

**Conclusion:** Findings demonstrate potential of MenB-fHbp containing vaccines to protect against ST-1161 strains associated with this outbreak, with hSBA results consistent with expected susceptibility based on fHbp-expression levels.

Funded by Pfizer.



#### **037.** GENETICALLY DISTINCT HAJJ AND SOUTH AMERICAN-RELATED STRAINS OF SEROGROUP W NEISSERIA MENINGITIDIS CAUSING INVASIVE MENINGOCOCCAL DISEASE IN ONTARIO, CANADA, JANUARY 1, 2015 TO JUNE 30, 2024

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**Introduction:** In response to an increase in IMD due to seroroup W *N. meningitidis* (MenW), we characterized the recent trends in MenW isolates from IMD cases in Ontario, Canada.

**Material:** IMD isolates recovered from patients in Ontario between January 1, 2015 and June 30, 2024 were included in this study.

**Methods:** IMD isolates were identified and serogrouped by the Public Health Ontario Laboratory. Ontario MenW isolates were compared with global MenW isolates by core-genome multilocus sequence typing (cgMLST).

**Results:** The percentage of culture-confirmed IMD caused by MenW in Ontario increased from 10.0% in 2015 to 40.9% in the first half of 2024, and consisted almost entirely of strains belonging to the ST-11 CC. Ontario MenW isolates were related to MenW from other countries when analyzed by cgMLST. Most Ontario MenW from prior to 2024 belonged to variants of the South American strain sublineage. However, a cluster of 8 MenW cases from 2024 in one city was caused by a strain related to the Hajj strain sublineage and found to be related to the international Umrah MenW outbreak strain described in May-June 2024. Most (60.0%) MenW IMD cases in Ontario occurred in individuals older than 40 years of age. The majority (83.3%) of the MenW isolates were predicted by whole genome sequence analysis to express antigens covered by the 4CMenB vaccine.

**Conclusions:** Multiple different introductions of international MenW strains was likely the cause for the recent shift in MenW IMD in Ontario, Canada.



#### **038.** MENINGOCOCCAL VACCINATIONS IN TAIWAN: POST-COVID CONSIDERATIONS

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**Introduction:** A post-COVID resurgence in the number of meningococcal cases has raised concerns. While serogroup B is the predominant cause of the disease, cases caused by previously less frequent serogroups are reported recently. We hereby discuss local longitudinal epidemiological data of invasive meningococcal disease (IMD) and immunization recommendations made by the Infectious Diseases Society of Taiwan.

**Methods:** We reviewed the published studies of IMD in Taiwan and searched information available on health authority's websites. The Society held several working group meetings and expert meetings for making recommendations for the prevention of IMD and the immunization strategy for both MenACWY-CRM and 4CMenB vaccinations.

**Results:** Most IMD cases are in previously healthy individuals. Meningococcal serogroup Y is predominant in Japan. Post-COVID cases rebound by serogroups Y and W are reported (eg, US and France, respectively). During 2003 to 2020 in Taiwan, individuals <5, 5-29, and ≥30 years of age accounted for 32.8%, 29.8%, and 37.3% of the 134 disease-causing serogroup B isolates.

**Conclusions:** For healthy individuals, outbreaks of IMD caused by both MenACWY and MenB can potentially be occurred. MenACWY-CRM or 4CMenB vaccinations or both are recommended for the increased risk populations, including students planning to study abroad, military recruits, students planning to move into dormitory or returning to school, people planning to join mass gathering activities, and smokers. For the high risk populations (i.e., individuals with certain underlying medical conditions), both MenACWY-CRM and 4CMenB vaccinations are recommended. Meningococcal vaccinations are recommended for the control of outbreaks, and the close contacts.





ANIZED B

### Session 8: Clinical aspects and management of IMD and IHiD

# **039.** EVERYTHING, EVERYWHERE, ALL AT ONCE: THE INCREASE OF ATYPICAL PRESENTATIONS OF INVASIVE MENINGOCOCCAL DISEASE IN FRANCE OVER THE LAST DECADE

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**Introduction:** Evolution of invasive meningococcal disease (IMD) cases is unpredictable with many successive trends and changes. The most impactful was the recent decline upon the implementation of non-pharmaceutical interventions (NPI) to control the COVID-19 pandemic follow by a rebound since 2022 in numbers with genotypical changes of the strains. We explored associated modifications in the clinical presentations of IMD.

**Material:** We conducted a retrospective descriptive study using the Database of the French National Reference Centre for meningococci and *Haemophilus influenzae* for IMD cases between 2014 and 2024. This represented a total of 4186 cases. We scored serogroups, sex, age groups, clinical presentations and clonal complexes of the corresponding patients and isolates. We performed Chi-squared tests and adjusted the threshold using the Bonferroni correction for multiple comparisons.

**Results:** Non-meningeal forms of IMD increased significantly upon easing of NPI, especially bacteremic meningococcal pneumonia (from 0.9% in 2014 to 7.3% in 2024) and abdominal forms (from 0.4% in 2014 to 6.7% in 2024). Both presentations almost doubled in average proportion since 2020. They were significantly linked to serogroups Y and W, to older adults for bacteremic pneumonia and to adolescents and young adults for abdominal presentations. These forms were significantly associated with more early mortality and clonal complexes 23, 11 and 9316.

**Conclusions:** The increase in atypical IMD forms may lead to higher burden of IMD due to delayed diagnosis and management. This increase contributed to change of the French policy makers to change the vaccination schedule in 2025, with a new adolescent-focused recommendation and a temporarily extended catch-up for children.



#### 040. IMPACT OF POINT-OF-CARE TESTING ON INVASIVE MENINGOCOCCAL DISEASE SURVEILLANCE IN ENGLAND: CHALLENGES FOR STRAIN TYPING AND STRATEGIES FOR MITIGATION

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**Introduction:** In recent years, Point-of-care testing (POCT) platforms for rapid meningitis diagnosis have been established in English microbiology labs. Such platforms often consume the limited samples, preventing strain characterisation— an important pillar of infectious disease surveillance and public health management. This study evaluates the impact of POCT on invasive meningococcal disease (IMD) surveillance in England and explores a method for improving sample recovery.

**Methods:** We compared local laboratory and national reference IMD datasets (April 2022–December 2024), alongside laboratory follow-up, to identify cases confirmed locally via POCT but not by the national reference laboratory. Additionally, we assessed sample recovery from the BIOFIRE<sup>®</sup> FILMARRAY<sup>®</sup> Meningitis/Encephalitis (ME) Panel (Biomerieux). DNA from ten diverse meningococcal strains was tested for detection from recovered material.

**Results:** Fifteen IMD cases were confirmed locally by POCT but lacked sufficient sample for national reference laboratory referral, with most (n=10) occurring in 2024, suggesting an increasing issue. The BIOFIRE<sup>®</sup> FILMARRAY<sup>®</sup> ME Panel detected all ten meningococcal strains, and successful further testing was achieved using extracted samples diluted in lysis buffer.

**Conclusions:** POCT use for meningitis diagnostics impacts meningococcal surveillance and public health response, with an increasing number of missed cases. Sample recovery from BIOFIRE sample tubes offers a potential solution to support ongoing strain characterisation.







ANIZED B

#### **041.** BIOFILM-ASSOCIATED HAEMOPHILUS INFLUENZAE IN GENITAL INFECTIONS: A POTENTIAL TARGET FOR THERAPEUTIC INTERVENTION

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**Background:** *Haemophilus influenzae* is increasingly implicated in women genital infections and septic abortion. This study characterizes *H. influenzae* isolates from genital sites and placenta, assessing their antibiotic resistance, genetic diversity, and biofilm-forming capacity.

**Methods:** We analyzed *H. influenzae* isolates received at the French National Reference Centre for Meningococci and *H. influenzae* (2017–2022). Selected isolates originated from women genital sites, placenta, and neonatal gastric fluids (<4 days old). Characterization included antibiotic susceptibility testing, serotyping, whole-genome sequencing, and biofilm formation assays.

**Results:** All 123 isolates were non-typeable. Amoxicillin/ampicillin resistance was found in 37.4%, with 12 isolates producing beta-lactamase. Resistance to third-generation cephalosporins, co-trimoxazole, and ciprofloxacin was detected in 16.2%, 16.3%, and 1.6% of isolates, respectively. Some exhibited multidrug resistance. Whole-genome sequencing revealed high genetic heterogeneity across 26 clonal complexes, with 15 isolates unassigned to known complexes. Biofilm-related gene analysis grouped isolates into subclusters, one of which, enriched with placental and neonatal gastric isolates, showed enhanced biofilm formation compared to isolates from non-pregnant women. Notably, biofilm formation was reduced using antibodies against the P5 protein, a key biofilm-associated factor.

**Conclusion:** Non-typeable *H. influenzae* isolates from genital infections exhibit genetic diversity and antibiotic resistance. Anti-biofilm therapies, particularly targeting P5, could be a promising approach, especially for drug-resistant strains.



## **042.** ATYPICAL PRESENTATIONS DUE TO *N. MENINGITIDIS* IN GREECE DURING THE POST COVID-19 ERA (2022-2024)

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**Introduction:** *N. meningitidis* can cause life-threatening diseases. Occasionally, it can be recovered from infections outside the bloodstream or central nervous system. Herein, we present two rare cases within the year 2024.

**Materials and methods:** Two cases of rare meningococcal infections were notified in patients aged 8 and 25 year old (*Case-1 & Case-2*) respectively. *Case-1* presented with an inflammatory fistula in the midline of the neck while, *Case-2* presented with swelling of the left knee. Although both cases presented with high fever, no neurological signs were observed. Both cases were laboratory identified by phenotypical (Gram stain, culture, serogrouping) and genotypical methods (MLST, PorA, FetA and WGS). Antibiotic susceptibility testing was carried out by MIC method.

**Results:** Both isolates were found to belong to serogroups X (MenX) and B (MenB) for *Case-1* and *Case-2* respectively. Genotypic analysis for porA, fetA and MLST revealed the following characteristics: MenX,: 18, 25-44, F5-5, 198cc (ST-823) and MenB: 7-1, 1, F3-3, 32cc (ST-7460). It is noteworthy that MenX was identified for the first time in Greece and fine typing revealed rare genotypic characteristics on such a rare manifestation. Both isolates were susceptible to cefotaxime, rifampicin, chloramphenicol and ceftriaxone, while they expressed reduced susceptibility to penicillin. Further, Case-2 was resistant to ciprofloxacin.

**Conclusions:** *N. meningitidis*, although rare, can be recovered from unusual sites and specimens. Clinicians and microbiologists should always be aware and consider meningococcus as a potential causative agent of infections other than meningitis and septicaemia.



## **043.** LABORATORY-CONFIRMED INVASIVE MENINGOCOCCAL DISEASE IN ENGLAND IN 2024: LINKAGE ANALYSIS OF MULTIPLE NATIONAL DATABASES

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 Centre for Neonatal and Paediatric Infections (CNPI), St. George's University of London (SGUL), London, UK

**Background:** Invasive meningococcal disease (IMD) is rare but has high associated morbidity and mortality. The UK Health Security Agency provides comprehensive IMD surveillance for England, with the Meningococcal Reference Unit (MRU) delivering laboratory confirmation for the national IMD dataset. We conducted a case audit assessing completeness of this dataset.

**Methods:** All national IMD dataset cases in 2024 were linked to NHS laboratory records (SGSS), clinically notified cases (CIMS), and Office for National Statistics (ONS) death records.

**Results:** The national IMD dataset included 357 cases: 312 MenB (87.4%), 26 MenW (7.3%), 12 MenY (3.4%), 4 MenC (1.1%) and 3 others (0.8%). Fifteen ONS deaths were recorded (CFR:4.2%). SGSS included 355/357 cases (>99%). Time between first SGSS sample and first MRU sample was 0 days in 40% of cases, within 7 days in 69%, and within 21 days in 98%. All 357 cases were notified and therefore recorded in CIMS. Fifteen additional cases were identified in SGSS and 21 in CIMS, nine of which matched across both datasets.

**Conclusions:** Over 90% of cases were confirmed by the MRU and included in the national dataset. However, 27 additional cases were identified across SGSS and CIMS, with point-of-care diagnostictesting used in ten of these. Serogroup remains unknown for 26/27 missing cases meaning, for those caused by MenACWY (10% of MRU cases), recommended vaccination of close contacts was missed. Timely referral of MRU samples, within 7 days, occurred in 69% of cases, but delays in other cases could delay serogrouping, and thus public health actions.



### Session 9: Strain molecular characterization

#### **044.** MOLECULAR AND WGS-BASED CHARACTERIZATION OF INVASIVE *NEISSERIA MENINGITIDIS* ISOLATES COLLECTED IN BELGIUM (2016-2022) AND MENB-FHBP VACCINE COVERAGE ESTIMATION OF SEROGROUP B

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**Introduction:** Invasive meningococcal disease (IMD) caused by *Neisseria meningitidis* can result in life-threatening meningitis and septicaemia. There are twelve serogroups of *N. meningitidis*, but most cases of IMD are caused by serogroups A, B, C, W, X and Y. In Europe, serogroup B (MenB) accounts for 51% of documented cases as recently reported by the European Centre for Disease Prevention and Control (ECDC). As a major cause of IMD, genomic surveillance of circulating MenB strains and assessment of the potential impact of vaccination programs could help inform public health policy.

**Material and Methods:** In this study, a collection of 493 strains was analysed, collected in Belgium by the National Reference Centre between 2016 and 2022. Slide agglutination was used for serogroup determination and whole genome sequencing (WGS) was used to further characterize these strains.

**Results:** The observed serogroups were: MenB (n=281), MenY (n=95), MenW (n=83), MenC (n=30), non-groupable isolates (n=2), MenE (n=1) and MenX (n=1). A higher prevalence of MenY and MenW was observed in older adults. MenB isolates were grouped into 110 sequence types (STs), 89 of which belonged to 16 clonal complexes (CCs). Coverage of the MenB-FHbp vaccine (Trumenba, bivalent rLP2086; Pfizer Inc, New York, NY, USA ipv Philadelphia) was predicted using the Meningococcal Deduced Vaccine Antigen Reactivity (MenDeVAR) index. Of the 281 MenB strains collected between 2016 and 2022, 89.1% (lower limit – upper limit: 78.6 - 100.0%) were predicted by MenDeVAR to be covered by the vaccine.

**Conclusions:** This study highlights the benefits of a pathogen surveillance program and the need for experimental characterisation of continuously evolving antigenic variants.



## **045.** 4CMENB VACCINE COVERAGE OF INVASIVE SEROGROUP B MENINGOCOCCI COLLECTED IN BELGIUM BETWEEN 2016 AND 2022

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**Introduction:** Neisseria meningitidis infections can result in life-threatening meningitis and septicaemia. In Europe, serogroup B (MenB) is the major cause of IMD, particularly in young children. Genomic surveillance of circulating MenB strains by whole genome sequencing (WGS) provides a rapid and comprehensive assessment of the potential impact of vaccination programs helping to inform public health policy.

**Material and Methods:** Here, we present a retrospective analysis of clinical cases of MenB IMD (n=311) as well as whole-genome sequencing results from the associated MenB strains (n=281) as identified by slide agglutination and recovered in Belgium from 2016 to 2022 by the Belgian NRC.

**Results:** Genomic analysis of 281 of these strains showed high genetic diversity of the antigen targets included in the 4-component meningococcal serogroup B (MenB) vaccine, 4CMenB (fHbp, PorA, NHBA and NadA) and at the 4CMenB Antigen Sequence Types (BAST) level. 23.5% (66/281) of isolates represented new antigen combinations and had yet to be assigned a BAST ID. Coverage of the 4CMenB vaccine was predicted using the genetic Meningococcal Antigen Typing System (gMATS), and the Meningococcal Deduced Vaccine Antigen Reactivity (MenDeVAR) index. Of the 281 MenB strains collected between 2016 and 2022, 79.5% (lower limit – upper limit: 68.0 – 91.5) were predicted to be covered by the vaccine by gMATS, and 80.7% (lower limit – upper limit: 66.5 – 95.4%) by MenDeVAR.

**Conclusions:** This study highlights the benefits of a pathogen surveillance program and the need for experimental characterisation of continuously evolving antigenic subvariants of *Neisseria meningitidis*.





ANIZED B

# 046. AN UPDATE ON THE ST-485 (ST-41/44 CLONAL COMPLEX) MENINGOCOCCAL GROUP B STRAIN IN ENGLAND: 2010-2024

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**Introduction:** Serogroup B (MenB) is the most common invasive meningococcal serogroup in England, and ST-485 (ST-41/44 clonal complex) is currently the most common MenB sequence type. Here we present an update on ST-485 strains within the wider epidemiological picture in England, as well as providing an antigenic and clinical overview.

**Methods:** Serotyping was performed using a dot-blot ELISA. Genome sequence analysis was performed using the Illumina platform with draft genomes submitted to the PubMLST *Neisseria* database. Subtyping of PCR-only strains was performed using PCR and Sanger sequencing directly from clinical specimens.

Clinical and patient information was collated by the UKHSA Immunisation and Vaccine Preventable Diseases Division.

**Results:** Between 2010 and 2024, three quarters of English MenB cases were caused by four predominant clonal complexes: ST-41/44 complex, ST-269 complex, ST-213 complex and ST-32 complex.

In this period, the proportion of ST-41/44 complex strains belonging to ST-485 increased substantially, and since 2021 this sequence type has been the most common among invasive MenB isolates. Over 80% of ST-485 strains had the subtype P1.12-1,16,37-1, however, an increasing number of P1.16-183-expressing strains have been isolated.

Strain coverage of the licenced MenB vaccines remains high among ST-485 strains due a predominance of Factor H-Binding Protein (fHbp) peptide 4, and Neisserial Heparin Binding Antigen (NHBA) peptide 2.

**Conclusion:** ST-485 is a strain that continues to expand across England causing sporadic cases and outbreaks. Vaccine strain coverage is reassuringly high, but continual strain surveillance is in place to detect any changes to this and other MenB strains.



#### 047. CHARACTERIZATION OF AN UNCOMMON SEQUENCE TYPE OF SEROTYPE B HAEMOPHILUS INFLUENZAE (Hib) CAUSING AN INCREASE IN INVASIVE DISEASE IN BRITISH COLUMBIA, CANADA

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**Introduction:** In British Columbia (BC), the average annual number of invasive Hib cases between 2009 and 2018 was 2.8 cases (range from 0 to 6). However, between 2020 and 2022, 34 invasive Hib cases were reported [1].

**Material:** *Haemophilus influenzae* (Hi) isolates identified by the Public Health Laboratory of BCCDC from January 1, 2010 to June 30, 2024 were used in this study.

**Methods:** Identification and serotyping was done by standard methods. MLST was carried out as described [2]. Whole genome sequence (WGS) of ST-231 Hib were compared using the genome comparator tool from PubMLST (https://pubmlst.org/organisms/haemophilus-influenzae). SNVphyl analysis was done using the SNVPhyl pipeline (v1.2.3) [3].

**Results:** Of the 84 invasive Hib isolates, 62 (73.8%) belonged to ST-231, and the rest belonged to other members of ST-6 CC. WGS was done on 58 case isolates of ST-231 Hib.

SNVphyl analysis divided them into two groups according to isolation dates: early (n = 18) and late (n = 39). As revealed by genome comparator, the number of gene differences amongst the 58 ST-231 Hib ranged from 10 to 54 genes while they showed 1661 to 1672 gene differences from Rd KW20. Gene alignment also showed a number of virulence genes with various number of tandem repeats suggestive of phase variations. In contrast to other Hib, ST-231 isolates were showing susceptibility to ampicillin and other antibiotics. There was only 1 ST-231 Hib recorded in PubMLST.

**Conclusions:** ST-231 Hib, an uncommon sequence type, has caused an increase in invasive disease in BC, Canada.

Reference:

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#### **048.** FAILURES OF *HAEMOPHILUS INFLUENZAE* B CONJUGATE VACCINES IN AGE-APPROPRIATELY VACCINATED CHILDREN UNDER 5 YEAR-OLD: FRANCE, 2017-2024

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**Introduction:** Despite the effectiveness and the high coverage rate of *Haemophilus influenzae* serotype b (Hib) conjugate vaccines, invasive Hib disease are reported among vaccinated children. This study describes clinical, microbiological and immunological features of invasive Hib disease among vaccine failure children < 5-y-olds identified between 2017-2024 in France.

**Methods:** A total of 268 Hib isolates were analysed at the National Reference Centre for *H. influenzae* that were analysed by whole genome sequencing. Sera at the admission and convalescent phases were obtained from vaccine failure children <5 years. Specific *H. influenzae* b IgG ELISA Kit was used to quantify anti-polyribosyl-ribitol phosphate (PRP) IgG antibodies. Functionality was addressed by opsono-phagocytosis and complement deposition assays.

**Results:** Among 268 identified Hib cases, 73.5% occurred in children < 5-year-olds. All these isolates belong to the clonal complex 6. Of 171 children <5-year-olds with known vaccine status, 84.0% received at least one vaccine dose and 31.6% cases were TVFs. Most vaccine failures children were lacking sufficient level of functional IgG anti-PRP antibodies at the acute phase of the disease to sustain long-term protection. This level increased markedly above the protective concentration of 1.0 mg/L in convalescent phase-sera.

**Conclusions:** These results clearly suggest that Hib vaccine failures in children were mostly associated with low titters of anti-PRP IgG suggesting that only 2 doses (primary schedule) and/or the absence of a booster during the second year of life may be questioned. Surveillance of cases and monitoring of titres need to be continued to inform future vaccination Policy.



### Session 10: Thinking out of the box

#### 049. INFLUENCE OF A FATAL CASE AS A COMPLICATION OF MENINGOCOCCAL DISEASE IN GREECE, ON HEALTHCARE WORKERS' ATTITUDE TOWARDS VACCINATION: A CROSS-SECTIONAL STUDY

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**Background:** Invasive Meningoccocal Disease (IMD) is a severe and potentially life threatening. The aim of the study is to evaluate how the latest 20 year old student fatal case due to IMD in Greece influenced the perspective regarding vaccination of healthcare professionals in Primary Health Care, for themselves and their children, Understanding these modifications is critical for developing public health policies and enhancing vaccination.

**Materials and Methods:** A cross-sectional study was carried out among 100 healthcare professionals working in Primary Health Care in Trikala city in the Region of Thessalia, Central Greece. Participants filled an anonymous questionnaire, regarding information on demographics immunization status, awareness of the event and intent to receive or recommend the vaccine.

**Results:** Among the participants, 30% responded that already received the MenB and 60% vaccinated their children against IMD. Remarkably, 100% of them were aware of the fatal case and 55% revealed that this incident modified their intentions to receive the vaccine and vaccinate their children. Furthermore, 65% agreed that meningococcal vaccination has to be introduced as obligatory vaccination for healthcare professionals. However, only 45% consider themselves as 'well-informed' or 'very well-informed' about meningococcal disease and vaccination, emphasizing critical disparities in education and awareness.

**Conclusion:** The recent fatal case, as a result of IMD complication, had significant impact on healthcare workers' willingness to be vaccinated against the disease. Nevertheless, the highlighted deficiencies in knowledge point out the urgent need for strategic educational interventions to strengthen the trust in meningococcal vaccines and promote higher immunization coverage among healthcare professionals.



## **050.** THE IMPACT OF THE COVID-19 PANDEMIC ON INVASIVE MENINGOCOCCAL DISEASE IN THE CZECH REPUBLIC

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**Introduction:** The aim of this study was to analyse the impact of the COVID-19 pandemic on the epidemiological situation of invasive meningococcal disease (IMD) and molecular characteristics of *Neisseria meningitidis* isolates causing IMD in the Czech Republic.

**Material and Methods:** The study was based on IMD surveillance data for 2018-2024 and all available *N. meningitidis* isolates from these years were subjected to whole genome sequencing (WGS). The studied years was divided into three periods: the pre-COVID, the COVID, and the post-COVID period.

**Results:** WGS characterisation showed a gradual change in the population of meningococci causing IMD in the Czech Republic during the COVID and post-COVID periods. For *N. meningitidis* isolates of serogroups C, W, and Y, a gradual and significant decline in overall heterogeneity was observed – from 10 different clonal complexes to only 3 in the post-COVID years (cc11, cc23, and cc103). At the same time, a significant reduction was detected in cc11 isolates. In contrast, an increase in overall heterogeneity was observed for *N. meningitidis* B isolates during the COVID period, followed by its decline again to overall lowest values in the post-COVID period.

**Conclusions:** Strong selection pressures can lead to significant changes in bacterial populations. This was also detected in the case of studied *N. meningitidis* isolates causing IMD in the Czech Republic during the COVID-19 pandemic.

Acknowledgement: The project "Genomic surveillance of selected infectious diseases in the Czech Republic" (Grant agreement no. 101113387 - HERA2CZ) is co-funded by the European Union.



# **051.** TROUBLED TIMES, CHANGING TIDES: A SEROPREVALENCE STUDY ON MENINGOCOCCAL IMMUNITY IN FRANCE BETWEEN 2016 AND 2024

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**Introduction:** In France, non-pharmaceutical interventions (NPIs) implemented to curb COVID-19 led to a spectacular decline in invasive meningococcal disease (IMD) cases. However, a rebound in cases, notably for serogroups W and Y, emerged after the gradual lifting of NPIs, raising questions about an "immunity gap" due to reduced circulation of the bacteria. During the study period, vaccination against MenC was mandatory in 2018 and recommended against MenB since 2022.

**Material:** We conducted a retrospective seroepidemiological study using 166 normal serum samples collected between 2016 and 2024.

**Methods:** Anti *N. meningitidis* IgG levels were quantified by ELISA using purified capsular polysaccharides for serogroups B, C, W, Y, and X. Samples were categorized into three periods: pre-NPIs (n = 72), during NPIs (n = 33), and post-NPIs (n = 61). Statistical comparisons were performed using Kruskal-Wallis tests for non-parametric data.

**Results:** Our results show a significant decline in anti-serogroup B IgG antibody levels after the lifting of NPIs (p < 0.0001), while anti-serogroup C IgG antibody levels incrementally increased (p = 0.0003), likely reflecting a catch-up in MCC vaccination coverage. Anti-serogroup W IgG antibody levels remained stable, suggesting sustained circulation potentially due to a genotypic shift. Anti-serogroup Y IgG antibody levels transiently increased significantly (p < 0.0001) during NPIs but then returned to pre-pandemic levels after their lifting. Anti-serogroup X IgG antibody levels remained stable, consistent with its low prevalence.

**Conclusions:** Our study demonstrates a heterogeneous impact of NPIs on *N. meningitidis* serogroup-specific immunity in France, that illustrates the complex interplay between public health interventions, vaccination policies, and meningococcal epidemiology.



### Session 11: Antibiotic resistance

#### **052.** EMERGENCE OF MULTIDRUG RESISTANT HAEMOPHILUS INFLUENZAE IN PORTUGAL: FIRST ISOLATE HARBORING EXTENDED-SPECTRUM BETA-LACTAMASE, BLACTX-M-15

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**Introduction and Aim:** Antimicrobial resistance (AMR) in *Haemophilus influenzae* is increasing globally, with limited reports on multidrug- and extensively drug-resistant isolates. This study analyses AMR in isolates collected at the National Reference Laboratory for *Haemophilus influenzae* from 2015 to 2024.

**Material and Methods:** The study included 439 isolates (267 invasive; 172 non-invasive infections), mostly retrieved from males (59.7%) and patients  $\geq$ 65 years (43.3%), with 30.7% from children  $\leq$ 5 years. Antimicrobial susceptibility was assessed phenotypically by beta-lactamase production and microdilution testing (EUCAST) and genotypically via whole-genome sequencing (Illumina). MLST and ftsl mutations were determined in silico.

**Results:** Beta-lactamase production was detected in 16.9% of isolates. In silico analysis showed 19.8% of invasive and 14.0% of non-invasive isolates carried beta-lactamase genes, mainly  $bla_{TEM-1B}$ . Three BLNAS invasive isolates carried inactive beta-lactamase genes. Of note, one multi-drug resistant (MDR) isolate carried both  $bla_{TEM-1B}$  and  $bla_{CTX-M-15}$  genes. *ftsl* mutations linked to  $\beta$ -lactam resistance were found in 30.8%, mostly gBLNAR-IIb. Resistance rates were 19.6% to ampicillin, 23.7% to cefuroxime, 31% to trimethoprim-sulfamethoxazole, and lower for other antibiotics. MDR occurred in 4.6% of isolates, with a sharp increase in 2024 (50.0%), including gBLNAR-III-like strains. International resistant clones were identified, including ST-103, ST-57, ST-836, ST-107 and ST-14 lineages. A surprising high genetic diversity (80.0%) was observed among MDR isolates.

**Conclusion:** AMR is alarming increasing in Portugal with a resurgence of MDR isolates in 2024. Notably we report the first MDR isolate carrying the extended spectrum beta-lactamase *bla*<sub>CTX-M-15</sub>, along with *bla*<sub>TEM-1B</sub>. These findings highlight the need for continued surveillance and urgent measures to contain the spread of resistance.



# **053.** β-LACTAM RESISTANCE AMONG *HAEMOPHILUS INFLUENZAE* ISOLATES RESPONSIBLE FOR INVASIVE INFECTIONS IN POLAND, 2018-2023

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**Introduction:** *Haemophilus influenzae* (Hinf) is a human-specific Gram negative bacterium responsible for respiratory tract infections, sepsis and meningitis. The study aimed to characterize the mechanisms of  $\beta$ -lactam resistance among invasive Hinf strains.

**Materials:** The study was conducted on 400 Hinf responsible for invasive infections, collected between 2018 and 2023 at the National Reference Center for Bacterial Meningitis (NRCBM).

**Methods:** All isolates underwent susceptibility testing and screening for  $\beta$ -lactam resistance mechanisms. Additionally, whole genome sequencing (WGS) analysis was conducted on a select group of isolates.

**Results:** Resistance to ampicillin, cefotaxime and meropenem was found in 6.0%, 1.0%, 4.5% isolates, respectively. Based on the screening test, 134 isolates were suspected of having a resistance mechanism to  $\beta$ -lactams. 66.5% of isolates were categorized as BLNAS ( $\beta$ -lactamase negative, ampicillin-susceptible), 17.8% as BLNAS with modified PBP3 (mutations in *ftsl* gene), 7.0% as BLNAR (-lactamase negative, ampicillin-resistant). Production of  $\beta$ -lactamase characterized 8.8% of isolates. According to the molecular classification of PBP3 alterations, 75.2% of BLNAR belonged to group II (representing four subgroups IIa-IId), 3.0% to group III, and 8.6% to like-III group. In the WGS analysis 50 distinct sequence types (STs) were identified; among isolates with altered PBP3 the most common was ST-107 (12.1%). BLPAR isolates predominantly represented ST-103/CC11 (51.7%).

**Conclusion:**  $\beta$ -lactam resistance among invasive Hinf isolates in Poland has remained stable over the years. Recently, however, resistance to third-generation cephalosporins has emerged. Effective detection methods, continuous surveillance, and a rational antibiotic policy are essential to address Hinf resistance.



#### **054.** ANTIBIOTIC RESISTANCE IN NON-INVASIVE HAEMOPHILUS INFLUENZAE ISOLATES FROM PATIENTS AT OUTPATIENT DEPARTMENTS IN GERMANY

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**Introduction:** *Haemophilus influenzae (Hi)* is a common cause of upper respiratory tract, ear and eye infections. These infections play a significant role in the prescription of antibiotics in the outpatient sector in Germany. We aimed to provide data on susceptibility rates for non-invasive clinical *Hi* isolates against oral antibiotics to guide decisions on empirical antimicrobial use.

**Methods:** A network of sentinel diagnostic laboratories across Germany collected clinical strains from ear, nose, throat, and eyes in 2019/2020 and 2022/2023. Antibiotic susceptibility testing was conducted using a commercial broth microdilution kit. All isolates were tested by nitrocefin disks to detect  $\beta$ -lactamases and subsequently positive isolates were characterized by TEM-1 PCR. To analyze molecular antibiotic resistance pattern resistance genome sequencing of the isolates from 2019/2020 was performed.

**Results:** The highest resistance rates were observed for amoxicillin (14% vs.13%), cefuroxime (18.6% vs. 20%) and trimethoprim/sulfamethoxazole (16% vs. 15%) in the 2019/2020 and 2022/2023 periods, respectively. Resistance to amoxicillin was mainly due to the -lactamase TEM-1 (96.7%). Additionally, one isolate was phenotypically -lactamase-negative amoxicillin resistant (BLNAR) and another isolate demonstrated -lactamase-negative amoxicillin clavulanic acid resistance (BLPACR). Resistance to 3rd generation cephalosporines was low (3,2% vs. 1%). Genome sequencing revealed that most cefuroxime-resistant isolates (97.5%) carried PBP3 mutations. All co-trimoxazole resistant isolates showed known *folA* mutations.

**Conclusions:** In general, resistance to oral antibiotics in clinical non-invasive *Hi* isolates is at a low level in Germany. Nevertheless, further monitoring of antimicrobial susceptibility is important to provide the database for guidelines on antibiotic use.





#### **055.** AN OVERVIEW OF CHARACTERISTICS AND ANTIBIOTIC SUSCEPTIBILITY PROFILES OF MENINGOCOCCAL AND HAEMOPHILUS INVASIVE DISEASE IN CROATIA (2023–2025)

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**Introduction:** Invasive diseases caused by *Neisseria meningitidis* (IMD) and *Haemophilus influenzae* (IHD) in Croatia have shown altered patterns following the COVID-19 pandemic. This study aims to analyze changes in age distribution and antibiotic susceptibility over the past two years.

**Materials and Methods:** Data from patients hospitalized at the University Hospital for Infectious Diseases (UHID) in 2023 and 2024 were analyzed. Key variables included age, seasonality, diagnostic methods, bacterial serogroups, and antibiotic susceptibility.

**Results:** Thirty patients were hospitalized (14 with IMD and 16 with IHD). Among IMD patients, 43% (6/14) were children aged 2-11 years, 35% were young adults (17-34 years), and 21% were 48 years or older. IHD was more common in patients aged 60 years and older (75%, 12/16). IMD cases peaked in spring and autumn, while IHD occurred year-round. Multiplex PCR was used in 50% of cases. *Neisseria meningitidis* serogroup B was most prevalent (5/10), primarily affecting children, while group Y was more common in adults. All *N. meningitidis* isolates were susceptible to penicillin and other tested antibiotics. *Haemophilus influenzae* was susceptible to all antibiotics tested, except sulfamethoxazole-trimethoprim.

**Conclusion:** The incidence of IMD and IHD in Croatia remains low, with IHD slightly increasing post-COVID-19. IMD cases have shifted toward young adults, especially *N. meningitidis* group Y. No antibiotic resistance was observed, indicating favorable treatment and chemoprophylaxis prospects.



#### 056. N. MENINGITIDIS SUSCEPTIBILITY TO PENICILLIN IN GREECE (2015-2023)

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**Introduction:** Invasive Meningococcal Disease (IMD) requires urgent antibiotic administration. Penicillin is one of the antibiotics, effectively used, since the vast majority of *N. Meningitidis* is highly susceptible. However, reduced susceptibility to penicillin is increasingly reported worldwide. This reduction has been directly linked to 5 critical amino acid substitutions that alter the structure of a meningococcal penicillin-binding protein (PBP2), encoded by the *penA* gene.

**Material:** DNA from meningococcal isolates and positive clinical samples obtained from 200 patients presented IMD during 2015-2023 were studied.

**Methods:** PCR and sequencing for *penA* gene was performed, directly in clinical samples as well as isolates and identification of the *penA* alleles with the aid of PubMLST database. E-test was performed in isolates.

**Results:** Pen<sup>s</sup> alleles (penicillin-susceptibility/standard exposure) decreased from 82.5% (2015) to 35.7% (2023)- predominant alleles *penA3* & *penA22* (14% each), *penA27* (9.5%). An increase was observed on the Pen<sup>I</sup> alleles (reduced susceptibility to penicillin/ increased exposure) from 10% (2015) to 57.14% (2023) (predominant alelles *penA14* (5.0%) and *penA12* (4.5%)). The overall penicillin-resistance due to Pen<sup>R</sup> was 13.4% (most frequent Pen<sup>R</sup> allele *penA295* (7.5%)). The majority of Pen<sup>R</sup> alleles were detected among the MenB (92.6%), whereas no resistance was detected for MenY.

**Conclusion:** This study summarizes susceptibility to penicillin in IMD patients throughout a 9-year period. It is the first study including data from isolates and direct application on clinical samples. From the above data, we conclude that genotypic monitoring of both antibiotic resistance and reduced susceptibility is important for monitoring IMD and antibiotic treatment.



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