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Antimicrobial susceptibility of invasive *Neisseria meningitidis,* 2022

The antimicrobial susceptibility of 43 viable meningococcal isolates received at ESR from cases of invasive disease were tested. Group, PorA and strain data was generated by the Invasive Pathogens Laboratory, ESR. Ceftriaxone, ciprofloxacin, penicillin and rifampicin minimum inhibitory concentrations (MICs) were determined by Etest on Mueller-Hinton agar + 5% sheep blood. MICs were interpreted according to Clinical and Laboratory Standards Institute (CLSI) breakpoints.[1] Meningococci with penicillin MICs ≥0.5 mg/L were categorised as resistant while those with MICs of 0.12 and 0.25 mg/L were categorised as intermediate.

The 43 meningococcal isolates tested for susceptibility included 35 group B isolates, six group Y isolates and two group W isolates. The most common group B strains were the B:P1.7-12,14 strain[a], with 15 isolates identified, and the B:P1.7-2,4 strain, with nine isolates identified.

14.0% (6/43) of isolates were categorised as penicillin resistant (i.e. MICs ≥0.5 mg/L) (Table 1). The prevalence of penicillin resistance in each of the meningococcal groups was:

- 11.4% (4/35) group B isolates, including
  - 26.7% (4/15) of the B:P1.7-12,14 strain
  - 0.0% (0/9) of the B:P1.7-2,4 strain
- 0.0% (0/6) group Y isolates
- 100.0% (2/2) group W isolates

Table 1. Antimicrobial susceptibility, MIC range and MIC_{90} of *N. meningitidis* from invasive disease cases, 2022

Antimicrobial	Percent (number)			MIC range (mg/L)	MIC_{90} (mg/L)
	Susceptible	Intermediate	Resistant		
Penicillin#	39.5 (17)	46.5 (20)	20.0 (6)	0.03-0.5	0.5
ceftriaxone	100 (43)	-^	-^	<0.002-0.004	0.004
rifampicin	100 (43)	0.0 (0)	0.0 (0)	0.008-0.12	0.06
ciprofloxacin	100 (43)	0.0 (0)	0.0 (0)	0.004-0.008	0.004

penicillin susceptible, MIC ≤0.06 mg/L; intermediate, MIC 0.12-0.25 mg/L; resistant, MIC ≥0.5 mg/L
^ there is no intermediate or resistant category for ceftriaxone

a The B:P.1.7-12,14 strain belongs to multilocus sequence type clonal complex 1572. In 2022 this included serogroup B isolates with the following PorA: P.1.7-12,14, P.1.7-36,14, P.1.7-12,15, P.1.7-13,14, and P1.7-12,16-3.

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60.5% (26/43) of isolates were penicillin non-susceptible (i.e. penicillin intermediate or resistant, with MICs ≥0.12 mg/L). The prevalence of penicillin non-susceptibility in each of the meningococcal groups was:

- 51.2% (22/43) group B isolates, including
  - 100% (15/15) of the B:P1.7-12,14 strain
  - none (0/9) of the B:P1.7-2,4 strain
- 67.7% (2/3) group Y isolates
- 100.0% (2/2) group W isolates

Please note that isolates categorised as penicillin intermediate by CLSI (i.e. penicillin MIC of 0.12 and 0.25 mg/L) would be categorised as penicillin susceptible using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints.[2] Isolates with a penicillin MIC ≥0.5 mg/L would be classified as resistant using both CLSI and EUCAST breakpoints.

Five *penA* mutations have been shown to have a high correlation with reduced penicillin susceptibility.[3] Our data confirmed the correlation between the presence of these mutations and penicillin non-susceptibility, however there was an area of uncertainty, where phenotype and genotype did not correlate. All isolates with wildtype *penA* had a penicillin MIC ≤ 0.12 mg/L. However one isolate with penicillin MIC of 0.06 mg/L and one isolate with a penicillin MIC of 0.12 mg/L had mutations associated with reduced penicillin susceptibility. The lack of correlation between phenotype and genotype for these two isolates may partially be explained by the margin of error associated with the MIC test and/or the presence of genetic mutations that are not expressed.

All 2022 isolates were susceptible to ciprofloxacin, ceftriaxone and rifampicin (Table 1).

In 2022 most cases of meningococcal disease were found in the North Island (31/43, 72.1%). Of the six penicillin resistant isolates identified, four were from cases in the North Island and two were from cases in the South Island. Of the 26 penicillin non-susceptible isolates, 20 were from cases in the North Island.

The proportion of penicillin-resistant isolates (MIC ≥0.5 mg/L) increased between 2013 and 2021, to a high of 56.0%, but decreased in 2022 to 14.0%. Prior to 2020 the incidence of meningococcal disease,[4] as well as the prevalence of penicillin resistance was increasing (Figure 1). This was driven by group W meningococci (Figure 2), many of which were penicillin resistant.[5,6] The B:P1.7-12.14 strain is now the dominant strain in New Zealand,[4] which is more likely to be penicillin intermediate than penicillin resistant, resulting in the overall rates of penicillin resistance decreasing. Penicillin non-susceptibility among New Zealand meningococci continues to increase, although fluctuations have been observed due to low case numbers.

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Figure 1. Penicillin non-susceptible *N. meningitidis* from invasive disease, 2013-2022

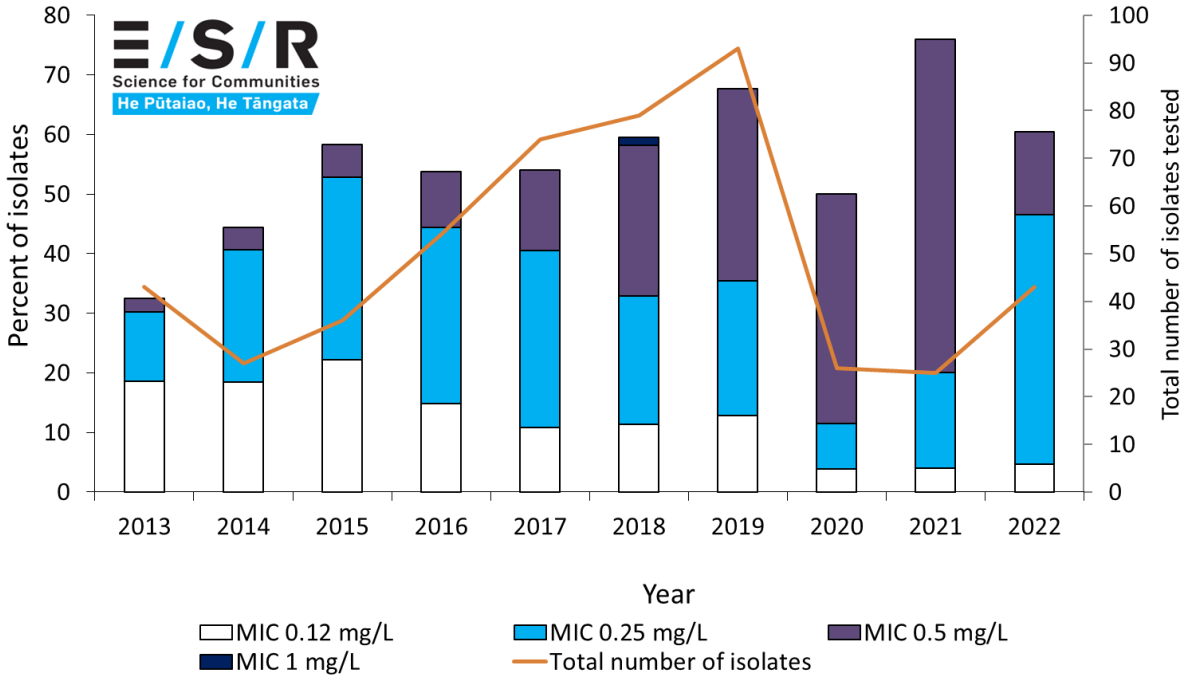
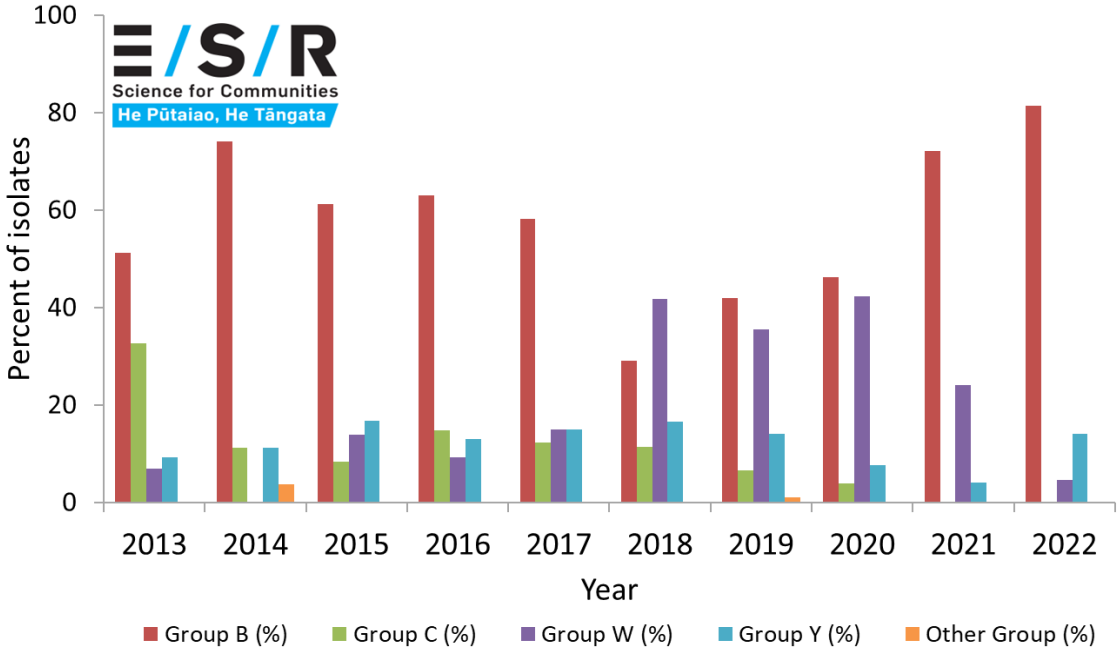


Figure 2. Distribution by group for isolates of *N. meningitidis* from invasive disease, 2013-2022. Adapted from data produced by the Invasive Pathogens Laboratory, ESR[4]



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Rifampicin resistance is rare among meningococci from invasive disease in New Zealand. In total, seven rifampicin-resistant isolates have been identified: one group C (C:2a:P1.5-1,10-1) isolate in 2011, one group B (B:4:P1.19,15) isolate and one group C (C:2a:P1.5-1,10-8) isolate in 2009, one group B (B:4:P1.4) isolate in 2003, one group C (C:2b:P1.2) isolate in 1997, one group B (B:15:P1.7,16) isolate in 1992, and one group A isolate in 1986.

Ciprofloxacin resistance is also rare among meningococci from invasive disease in New Zealand. In total three ciprofloxacin-resistant isolates have been identified: group C meningococci in 2010 (C:P1.20,23-7) and 2017 (C:P1.5,2) as well as a group X meningococcus in 2018.

No resistance to ceftriaxone has ever been identified among meningococci isolated from cases of invasive disease in New Zealand.

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1 Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 32nd ed. Wayne, USA: CLSI; 2022. CLSI supplement M100.

2 European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 12; 2022 January. Available from: https://www.eucast.org/

3 Thulin S, Olcén P, Fredlund H, Unemo M. Total variation in the *penA* gene of *Neisseria meningitidis:* correlation between susceptibility to beta-lactam antibiotics and *penA* gene heterogeneity. Antimicrob Agents Chemother. 2006 Oct;50(10):3317-24.

4 ESR, Invasive meningococcal disease report 2022. Accessed from: https://esr2.cwp.govt.nz/our-research/nga-kete/infectious-disease-intelligence

5 ESR, Antimicrobial susceptibility of invasive meningococcal disease, 2018. Accessed from: https://esr2.cwp.govt.nz/our-research/nga-kete/infectious-disease-intelligence.

6 ESR, Antimicrobial susceptibility of invasive meningococcal disease, 2019. Accessed from: https://esr2.cwp.govt.nz/our-research/nga-kete/infectious-disease-intelligence.

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