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ANTIMICROBIAL RESISTANCE IN STREPTOCOCCUS PNEUMONIAE FROM CASES OF INVASIVE DISEASE, 2022–2024

Authors: Andrea McNeill, Andrew Anglemyer, Charlotte Allen, Elena Cremm, Hannah Cooper, Kristin Dyet, Shamma Santa Agata

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SUMMARY

This report summarises the results of the laboratory surveillance undertaken by PHF Science of antimicrobial resistance in *Streptococcus pneumoniae* from cases of invasive disease in Aotearoa New Zealand (NZ) between 2022 and 2024 and supplements the Invasive pneumococcal disease reports 2022–2024[1-3].

The proportion of pneumococcal isolates in New Zealand that are penicillin resistant remained stable between 35–40% from 2022-2024.

Serotype 19A continues to make up approximately 75% of resistant isolates. Penicillin resistance among serotype 19A isolates increased from 54.4% in 2015 to 92.7% in 2023, before decreasing to 84.6% in 2024.

Cefotaxime resistance has remained relatively low from 2022–2024 (ranging from 0.3 to 2.7%). It is important to maintain antimicrobial susceptibility surveillance testing of cefotaxime due to its importance in clinical treatment of meningitis.

BACKGROUND

This report outlines the results and trends of antimicrobial resistance in S. *pneumoniae* isolates from cases of invasive pneumococcal disease (IPD) spanning 2022 to 2024. IPD refers to disease due to S. *pneumoniae* entering a sterile site, such as blood, pleural fluid, or cerebrospinal fluid. It has been a notifiable disease in New Zealand since 17 October 2008. IPD is largely a vaccine preventable disease, with vaccines available that provide protection against different serotypes of the bacterium. Following several changes to the vaccine programme in recent years [2], PCV13 was re-introduced to the immunisation schedule in November 2022 in response to increasing incidence of disease caused by serotype 19A.

Recent epidemiology of IPD in New Zealand is summarised in the PHF Science Invasive Pneumococcal Disease Annual Report 2024[3]. In brief, IPD incidence in New Zealand slightly decreased in 2024 (13.5 cases per 100,000) compared to 2023 (14.5 cases per 100,000), though incidence remained high compared with 2014–2022. Incidence is highest among adults aged 65 and older. Incidence in children under 5 years of age has decreased since the re-introduction of PCV13. In 2024, cases due to serotype 19A decreased in all age groups, and incidence of IPD due to serotype 19A in children aged <2 years decreased to below 2020 levels. However, serotype 19A remains the most common serotype causing disease in New Zealand (approximately 26% in 2024), followed by serotype 8 and serotype 3. Māori and Pacific peoples continue to carry a much higher burden of disease than other ethnicities; this is evident for all age groups, but particularly among children under 2 years of age and adults 65 years of age or older.

Surveillance of antimicrobial susceptibility of case isolates is essential to:

- Inform empiric treatment; and
- Inform immunisation policy, with the intention of achieving protection against serotypes with increasing antimicrobial resistance.

METHODS

In this report, the data presented for 2022–2024 is based on IPD case notifications supplemented with typing and antimicrobial susceptibility data from PHF Science's national reference laboratory. Diagnostic microbiology laboratories in NZ are requested to refer all invasive isolates of S. *pneumoniae* (i.e. isolates from cerebrospinal fluid, blood, or other normally sterile sites) to PHF Science for typing and antimicrobial susceptibility testing. A representative sample (in terms of serotype and age group) of isolates undergo antimicrobial susceptibility testing. In 2022 and 2023, isolates collected throughout the year were selected for susceptibility testing. In 2024 only isolates collected from January to September, inclusive, were tested.

Penicillin and cefotaxime susceptibilities were determined by Etest (bioMerieux, France) with European Committee on Antimicrobial Susceptibility Testing (EUCAST) Mueller-Hinton Fastidious agar and incubation for 20–24 hours at 35ºC with 5% CO_2. Data were interpreted using both meningitis and non-meningitis break points. Chloramphenicol, clindamycin, co-trimoxazole, erythromycin, moxifloxacin, rifampicin, tetracycline and vancomycin susceptibilities were determined by EUCAST disc susceptibility testing methods[5]. Inducible clindamycin resistance was detected by the D-zone test[4]. All minimum inhibitory concentrations (MICs) and zone of inhibition diameters were interpreted according to current EUCAST clinical breakpoints[5-7] from the year the sample was collected. EUCAST epidemiological cut-off (ECOFF) values were used if breakpoints were not available (available at www.eucast.com).

The antimicrobial susceptibility data for 2015 isolates is based on CLSI methods and breakpoints[8-11]. EUCAST breakpoints, where they differ from CLSI breakpoints, have not been retrospectively applied to MICs and zone diameters determined by CLSI methods due to differences between the two methods.

Multidrug resistance (MDR) was defined as resistance to three antibiotics, in addition to penicillin. When defining MDR, the meningitis breakpoints for penicillin were used.

RESULTS

The percentage of notified IPD cases with antimicrobial susceptibility testing (AST) results by year is 47.1% (297/631) in 2022, 45.8% (347/757) in 2023, and 37.3% (268/718) in 2024.

From 2022 to 2024, overall penicillin resistance (meningitis breakpoints) remained relatively stable, at 39.4% in 2022, 38.0% in 2023 and 35.4% in 2024 (Table 1). Among the penicillin-resistant isolates (meningitis breakpoints), the percentage that were multi-resistant to at least three additional antimicrobials, most commonly co-trimoxazole, erythromycin, and tetracycline or clindamycin, remained relatively low; 7.7% (9/117) in 2022, 3.0% (4/132) in 2023 and 2.1% (2/95) in 2024. The most common serotypes that were multi-resistant were 15A (n=4) and 19A (n=3).

Cefotaxime resistance (meningitis breakpoints) remained low, at 2.7% in 2022, 0.3% in 2023 and 1.9% in 2024. The serotypes of the isolates found to be cefotaxime-resistant from 2022 to 2024 were 7B, 9V, 14, 15A, 15B, 19A (n=3), 19F, 23B, 34, and 35B.

Table 1. Antimicrobial susceptibility among isolates from invasive pneumococcal disease cases, 2022–2024

Antimicrobial	2022 (N=297)			2023 (N=347)			2024 (N=268)		
	Susceptibility, % (n)			Susceptibility, %, (n)			Susceptibility, %, (n)		
	S[a]	I[a]	R[a]	S[a]	I[a]	R[a]	S[a]	I[a]	R[a]
Penicillin									
meningitis	60.6 (180)	-	39.4 (117)	62.0 (215)	-	38.0 (132)	64.6 (173)	-	35.4 (95)
non-meningitis	60.6 (180)	37.7(112)	1.7 (5)	62.0 (215)	37.8 (131)	0.3 (1)	64.6 (173)	35.4 (95)	0.0 (0)
Cefotaxime									
meningitis	97.3 (289)	-	2.7 (8)	99.7 (346)	0.0 (0)	0.3 (1)	98.1 (263)	-	1.9 (5)
non-meningitis	97.3 (289)	2.4 (7)	0.3 (1)	99.7 (346)	0.3(1)	0.0 (0)	98.1 (263)	1.9 (5)	0.0 (0)
Chloramphenicol[b]	99.3 (295)	-	0.7 (2)	99.4 (345)	-	0.6 (2)	100 (268)	-	0.0 (0)
Clindamycin[c]	96.0 (285)	-	4.0 (12)	93.7 (325)	-	6.3 (22)	95.5 (256)	-	4.5 (12)
Co-trimoxazole	65.3 (194)	1.3 (4)	33.3 (99)	64.3 (223)	1.7 (6)	34.0 (118)	66.8 (179)	2.2 (6)	31.0 (83)
Erythromycin[d]	93.3 (277)	0.3 (1)	6.4 (19)	92.5 (321)	-	7.5 (26)	93.3 (250)	-	6.7 (18)
Moxifloxacin	100 (297)	-	0.0 (0)	100 (347)	-	0.0 (0)	100 (268)	-	0.0 (0)
Rifampicin	100 (297)	-	0.0 (0)	100 (347)	-	0.0 (0)	99.6 (267)	-	0.4 (1)
Tetracycline[e]	92.3 (274)	0.3 (1)	7.4 (22)	93.4 (324)	-	6.6 (23)	92.2 (247)	-	7.8 (21)
Vancomycin	100 (297)	-	0.0 (0)	100 (347)	-	0.0 (0)	100 (268)	-	0.0 (0)

[a] S: susceptible, standard dosing regimen, I: susceptible, increased exposure, and R: resistant.

[b] The interpretation of susceptibility data for *S. pneumoniae* and chloramphenicol changed from R < 21 mm in 2022 to an ECOFF < 21 mm in 2023 and 2024.

[c] The percentage resistant given is for constitutive clindamycin resistance. Two isolates in 2022 and one isolate in 2023 had inducible clindamycin resistance.

[d] The breakpoint for *S. pneumoniae* and erythromycin changed from R < 19 mm in 2022 to R < 22 mm in 2023 and 2024.

[e] The breakpoint for *S. pneumoniae* and tetracycline changed from R < 22 mm in 2022 to R < 25 mm in 2023 and 2024.

In 2022, penicillin resistance (meningitis breakpoints) was highest in children aged 2–4 years (73.7%), followed by children aged <2 years (66.7%) (Table 2). IPD case numbers decreased in 2023 and 2024 among children aged <5 years and so few isolates were tested in these age groups, limiting interpretation of the susceptibility data. Among cases aged 5–64 years, the proportion of isolates with penicillin resistance remained fairly stable from 2022 to 2024. Among adults aged ≥65 years, the proportion with penicillin resistance was also fairly stable, ranging from 37.2% to 40.3%.

Cefotaxime resistance remains low, with the age group most affected with resistance being the ≥65 years age group.

Table 2. Penicillin and cefotaxime resistance among isolates from invasive pneumococcal disease cases, 2022-2024

Age group (years)	2022					2023					2024				
	Isolates	Penicillin		Cefotaxime		Isolates	Penicillin		Cefotaxime		Isolates	Penicillin		Cefotaxime	
		R[a]	%[b]	R[a]	%[b]		R[a]	%[b]	R[a]	%[b]		R[a]	%[b]	R[a]	%[b]
<2	21	14	66.7	0	-	9	3	33.3	0	-	4	3	75.0	0	0.0
2–4	19	14	73.7	0	-	14	11	78.6	0	-	5	2	40.0	0	0.0
5–64	139	44	31.7	3	2.2	187	67	35.8	1	0.5	135	40	29.6	2	1.5
³65	118	45	38.1	5	4.2	137	51	37.2	0	-	124	50	40.3	3	2.4
Total	**297**	**117**	**39.4**	**8**	**2.7**	**347**	**132**	**38.0**	**1**	**0.3**	**268**	**95**	**35.4**	**5**	**1.9**

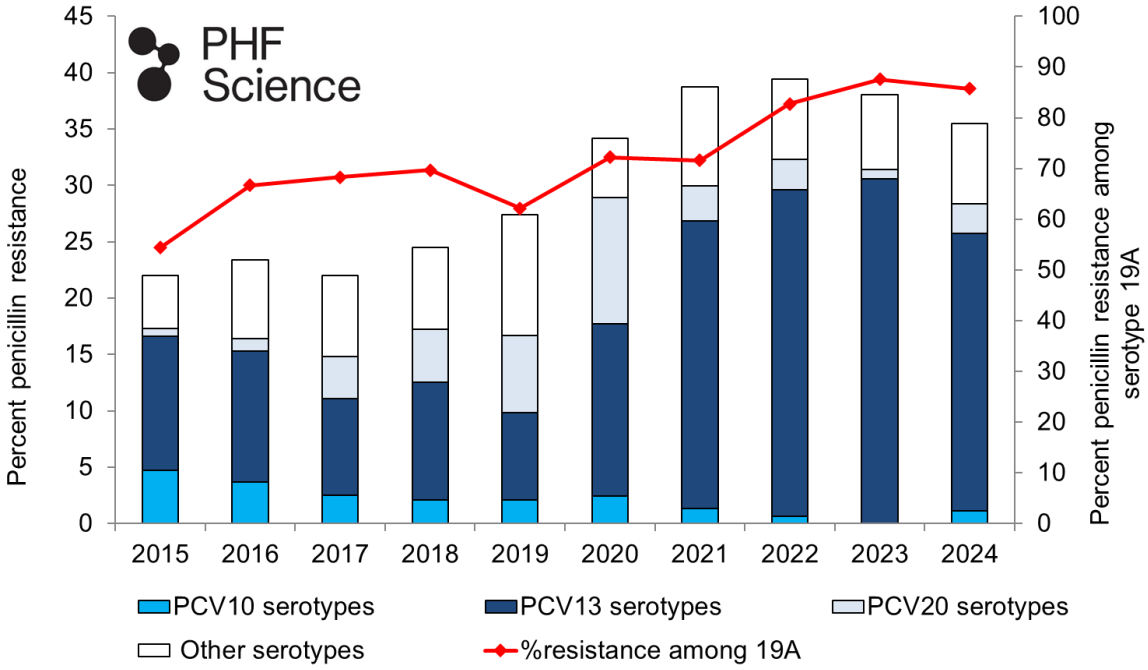
[a] R: resistant.

[b] Percentage of the isolates from the cases within the age group.

Penicillin resistance in *S. pneumoniae* from invasive disease has increased over the last decade (Figure 1). Following relatively stable resistance from 2015 to 2018 (approximately 22–25%), penicillin resistance increased from 2019, driven both by in an increase in the prevalence of serotype 19A isolates, and by increasing penicillin resistance among 19A isolates.

Since 2022, about 35–40% of all isolates from invasive pneumococcal disease have been penicillin-resistant, of which about 75% are specifically serotype 19A (Figure 1). Penicillin resistance among serotype 19A isolates increased from 54.4% in 2015 to 87.6% in 2023, before decreasing to 85.7% in 2024. Of the 36 isolates (2022–2024) that were resistant to more than one antimicrobial, nearly two-thirds were either serotype 19A (36%) or 15A (28%).

Figure 1. Penicillin-resistance amongst pneumococci from invasive disease cases, 2015–2024



Note: Serotypes covered by PCV10 include 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F. Additional serotypes covered by PCV13 include 3, 6A, 19A; Additional serotypes covered by PCV20 (excluding PCV13 serotypes) 8, 10A, 11A, 12F, 15B, 22F, 33F.

CONCLUSION

From 2022-2024, the proportion of tested S. *pneumoniae* isolates with resistance to penicillin has remained around 35–40%. Serotype 19A cases make up a large proportion of resistant isolates in New Zealand, due to both the high proportion of serotype 19A cases and high antimicrobial resistance within this serotype [12-13]. Following the re-introduction of PCV13 to the childhood vaccination schedule in 2022, there has been a reduction in incidence in 19A cases among children <5 years in 2023 and 2024. It is expected that indirect protection of older children and adults will reduce overall 19A case numbers within the next few years. This is expected to lead to a reduction in the prevalence of penicillin resistance among invasive pneumococci isolates.

Cefotaxime resistance has also been stable though at much lower levels (<3%). Cefotaxime is an important treatment option for invasive pneumococcal disease and monitoring susceptibility is important for informing empiric antimicrobial choices.

Penicillin resistance remains highest in young children, particularly in the 2–4 year age group in 2022-2023, likely due to high prevalence of 19A in this age group, who did not receive PCV13. Over the three years of this report, penicillin resistance has declined slightly overall, but still remains high across all age groups. Cefotaxime resistance remained low and stable over the 2022–2024 period, but it remains important to monitor due to cefotaxime's clinical use in meningitis treatment.

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NEW ZEALAND INSTITUTE
FOR PUBLIC HEALTH AND
FORENSIC SCIENCE LIMITED

- **Kenepuru Science Centre**
  34 Kenepuru Drive, Kenepuru, Porirua 5022
  PO Box 50348, Porirua 5240
  New Zealand
  T: +64 4 914 0700
- **Mt Albert Science Centre**
  120 Mt Albert Road, Sandringham, Auckland 1025
  Private Bag 92021, Auckland 1142
  New Zealand
  T: +64 9 815 3670
- **Wallaceville Science Centre**
  66 Ward Street, Wallaceville, Upper Hutt 5018
  PO Box 40158, Upper Hutt 5140
  New Zealand
  T: +64 4 529 0600
- **Christchurch Science Centre**
  27 Creyke Road, Ilam, Christchurch 8041
  PO Box 29181, Christchurch 8540
  New Zealand
  T: +64 3 351 6019

www.phfscience.nz