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Carbapenemase-producing organisms in New Zealand, 2023

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DISCLAIMER

CONTENTS

LIST OF TABLES

LIST OF FIGURES

EXECUTIVE SUMMARY

- Carbapenem-resistant Enterobacterales and *Pseudomonas* spp. are a major global health concern and remain World Health Organization (WHO) priority pathogens.
- The presence of these carbapenemase genes significantly limits treatment options due to activity against many β-lactam antibiotics.
- The burden of carbapenemase-producing organisms (CPO) in New Zealand is increasing. This is most notable for carbapenemase-producing Enterobacterales (CPE), with the majority of the increase due to increasing numbers of carbapenemase-producing *Escherichia coli*.
- The predominant carbapenemase genes in CPE in 2023 were NDM and OXA-48-like.
- The number of CPE with more than one carbapenemase gene increased. The most common combination was isolates with both an NDM and OXA-48-like gene.
- The predominant carbapenemase found in carbapenemase-producing *Pseudomonas* spp. (CPP) in 2023 were NDM and VIM.
- Genomic analyses indicate that whilst there is significant variation and diversity in the CPO identified in New Zealand, many of the globally recognised “high-risk clones” are present.
- There was transmission of CPE in New Zealand in 2023, supported by both epidemiological investigations and genomic clustering analyses. This highlights the importance of ongoing genomic surveillance of these hospital-associated pathogens.
- Prospective, continuous surveillance must continue in order to promptly identify future transmission events.
- Diagnostic laboratories must be supported to continue to refer suspected CPO to PHF Science for characterisation.

BACKGROUND

Acquired carbapenem resistance in gram-negative pathogens is a major, on-going public health concern due to the high morbidity and mortality associated with these infections.[1] Carbapenemase genes confer resistance to carbapenems, that are often reserved for treating severe bacterial infections, and many other β-lactams antibiotics. Carbapenemase genes are commonly found on plasmids, along with genes conferring resistance to multiple other classes of antimicrobials, leading to multidrug-resistance.[2] Such plasmids can frequently transfer between bacteria and play a critical role in the spread of antimicrobial resistance.

The acquired or transferable carbapenemases found in gram negative bacteria belong to three of the four major classes of β-lactamases: classes A, B and D.[2]

- Ambler class A includes KPC and GES enzymes.
- Ambler class B are metallo-β-lactamases (MBLs), which include NDM, VIM and IMP.
- Ambler class D includes the OXA-23, OXA-40, OXA-48 and OXA-51 groups of β-lactamases.

In New Zealand, diagnostic microbiology laboratories are requested to refer all suspected carbapenemase-producing organisms (CPO) to PHF Science for confirmation and further investigation. This report summarises the characteristics of carbapenemase-producing Enterobacterales (CPE) and carbapenemase-producing *Pseudomonas* spp. (CPP) in 2023.

Reports on CPE and CPP confirmed between 2009, when the first isolate was identified in New Zealand, and 2022 are available on the PHF Science website at https://www.phfscience.cri.nz/expertise/public-health/antimicrobial-resistance.

METHODS

Diagnostic microbiology laboratories are asked to refer all suspected CPO to PHF Science. Duplicate isolates were excluded. Non-duplicate isolates, with a carbapenemase gene detected by the referring laboratory, underwent Illumina-based whole genome sequencing (WGS). Select isolates, including all isolates with an IMI carbapenemase, were also characterised using Nanopore-based long-read WGS to determine the location of the carbapenemase gene. Isolates with chromosomally-located carbapenemase genes were excluded from this report.

For WGS analysis, genomic DNA was extracted using the Roche High Pure PCR template preparation kit or the Chemagic 360 (Perkin Elmer). DNA libraries were created using the plexWell Library Preparation kit (SeqWell) or the gDNA Rapid Barcoding kit (Oxford Nanopore Technologies), and sequencing was performed using Illumina or Nanopore technology. Illumina data were analysed using an in-house developed pipeline linking together open-source packages and in-house scripts, which enables the carbapenemase gene subtype, the acquired resistome and the multilocus sequence type to be determined. Open-source packages included mlst v2.19.0[3], AMRfinderplus v4.0.3[4] and Mob Suite v3.1.6.[5] Nanopore sequencing data were assembled using Flye.[6] Hybrid Illumina and long-read assembly was performed using Pilon.[7] To investigate the genomic relatedness of isolates, core genome multilocus sequence typing (cgMLST) was performed using chewBBACA v.3.2.0[8] for *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* using the schemas available at https://www.cgmlst.org/ncs. SNP typing using either core genome SNP analysis (Snippy v. 4.6[9]) or Split Kmer analysis (SKA v. 1.0[10]) was performed to provide further resolution of clusters where required.

Suspected CPO isolates that were carbapenemase PCR negative, or not tested using PCR by the referring laboratory, were characterised using phenotypic testing and the modified carbapenemase inactivation method (mCIM).[11] A selection of the following PCRs may have been used, depending on screening results: KPC, IMI, GES, NDM, IMP, VIM, GIM, SIM, SPM and OXA.[12,13,14,15,16,17,18] A PCR for the chromosomally-located POM gene was also performed on select isolates.[19] Isolates positive in any of these tests, except the POM PCR, underwent Illumina-based sequencing.

RESULTS

CARBAPENEMASE-PRODUCING ENTEROBACTERALES

A total of 202 distinct CPE were isolated from 176 patients in 2023 (Figure 1 and Table 1). Species were predominantly *E. coli* (80.2%, 162/202), followed by *K. pneumoniae* (11.4%, 23/202). Sixteen patients had two distinct CPE, three patients had three distinct CPE, and one patient had four distinct CPE (see Table 1, footnote 1). Both the number of CPE and the number of patients CPE were isolated from increased in 2023 compared to 2022. The increase was largely due to an increase in the number of carbapenemase-producing *E. coli*, rising from 50 in 2022[20] to 162 in 2023. By contrast the number of carbapenemase-producing *K. pneumoniae,* which was the second most common species, stayed reasonably constant with 22 isolates in 2022 and 23 in 2023. The increase in CPE may be partially attributable to the New Zealand border being open for a full 12 months in 2023, as SARS-CoV-2 pandemic travel restrictions were gradually lifted during 2022.

Of the CPE confirmed in 2023 the sample source was provided for 99.5% (201/202) of the isolates. Of those with known source, 74.6% (150/201) were isolated from screening specimens. Among the 52 CPE from clinical specimens 80.4% (41/51) were from urinary sources, 15.7% (8/51) were from sterile sites, 2.0% (1/51) were from respiratory specimens and 2.0% (1/51) were from a skin and soft tissue infections.

Laboratories from the Auckland region referred the majority of confirmed CPE isolates (142, 70.3%). The only other laboratories to refer more than 10 CPE in 2023 were Awanui Labs Wellington (formerly Wellington SCL) (16, 7.9%), Awanui Labs Dunedin (formerly Southern Community Laboratories) (14, 6.9%) and Canterbury Health Laboratories (12, 5.9 %). 39.1% of CPE were from patients ≥65 years of age, 25.7% of cases among 45-64 year olds, 29.2% of cases among 15-44 year olds, and 5.9% under 15 years of age.

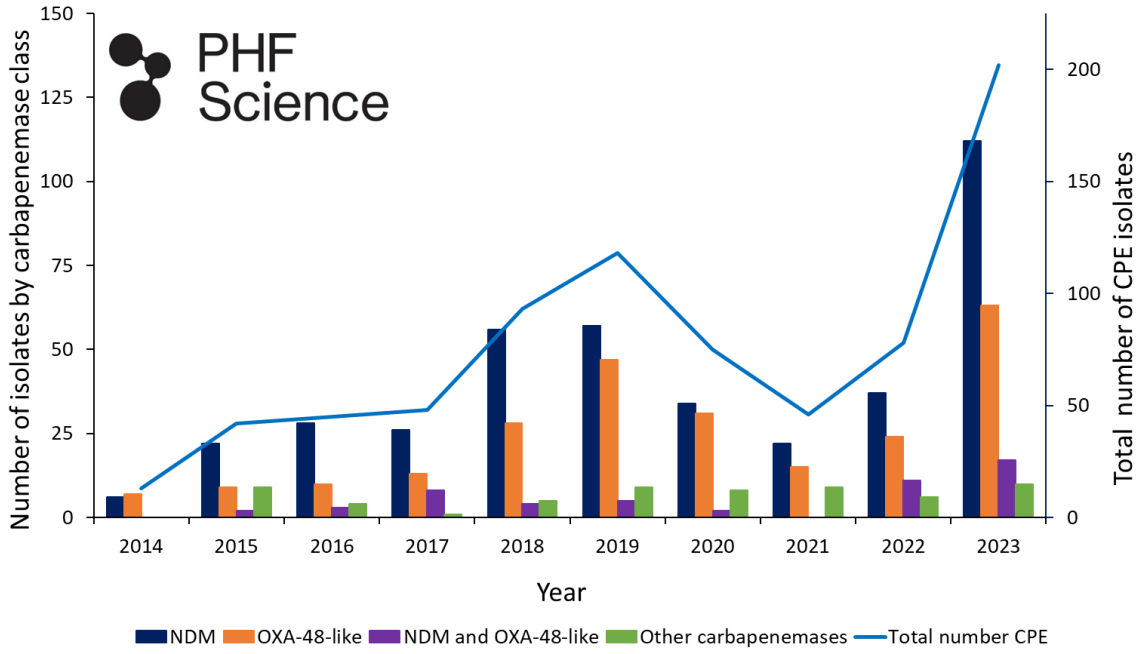

FIGURE 1: Number of carbapenemase-producing Enterobacterales (CPE) isolates identified in New Zealand, by carbapenemase class, from 2014 to 2023

Types of carbapenemase genes identified

As observed in previous years, the most frequently identified carbapenemase genes were MBL, with various subtypes of NDM found in 64.4% (130/202) of all CPE with carbapenemase genes in 2023 (Figure 1 and Table 1) and 59.6% (466/782) of all CPE in New Zealand to date. There were six isolates with an IMP carbapenemase gene found in 2023 (3.0%, 6/202), but no VIM genes. Together IMP and VIM MBLs have accounted for 3.1% (24/782) of all CPE identified in New Zealand to date.

OXA-48-like genes were the second most common carbapenemase gene identified in New Zealand CPE in 2023. They were found in 39.6% (80/202) of all CPE in 2023 (Table 1) and 38.7% (303/782) of all CPE in New Zealand to date.

A total of four other acquired carbapenemase genes were found in New Zealand CPE in 2023. Three isolates contained OXA-23, which is a gene more commonly found in *Acinetobacter calcoaceticus–baumannii* complex, but have been found in 15 CPE isolated in New Zealand to date. One further isolate contained a KPC gene, which have been found in 2.8% (22/782) of all CPE in New Zealand to date, of which 19 were in *K. pneumoniae* and one was in each of an *E. coli*, an isolate belonging to the *Enterobacter cloacae* complex, and a *Klebsiella oxytoca*.

TABLE 1: Types of carbapenemase genes identified among carbapenemase-producing Enterobacterales by species, 2023

Carbapenemase type and subtype	Number of isolates per species					All species
	Escherichia coli	*Klebsiella pneumoniae*	*Enterobacter cloacae* complex	*Citrobacter* spp.	Other species	
NDM	**92**	**10**	**3**	**5**	**2**	**112**
NDM-1	3	1	2	2[1]	1[3]	9
NDM-5	86	9	1	3[2]	1[4]	100
NDM-7	1	0	0	0	0	1
NDM-13	1	0	0	0	0	1
NDM-90	1	0	0	0	0	1
OXA-48-like	**57**	**4**	**1**	**0**	**0**	**62**
OXA-48	14	3	0	0	0	17
OXA-181	26	1	1	0	0	28
OXA-244	7	0	0	0	0	7
OXA-484	9	0	0	0	0	9
OXA-1181	1	0	0	0	0	1
NDM and OXA-48-like	**11**	**7**	**0**	**0**	**0**	**18**
NDM-1 and OXA-232	0	3	0	0	0	3
NDM-5 and OXA-181	7	2	0	0	0	9
NDM-5 and OXA-232	0	1	0	0	0	1
NDM-5 and OXA-484	1	0	0	0	0	1
NDM-5 and OXA-1181	1	0	0	0	0	1
NDM-5 and OXA-1205	1	0	0	0	0	1
NDM-5 and OXA-1207	1	0	0	0	0	1
NDM-1, NDM-5 and OXA-232	0	1	0	0	0	1
Other carbapenemase genes	**2**	**2**	**4**	**1**	**1**	**10**
IMP-4	0	2	4	0	0	6
KPC-3	0	0	0	0	1[5]	1
OXA-23	2	0	0	11	0	3
Total	**162**	**23**	**8**	**6**	**3**	**202[6]**

Footnotes Table 1

1. *Citrobacter freudii*
2. One of each of *Citrobacter freudii, Citrobacter braakii,* and *Citrobacter koseri.*
3. *Proteus mirabilis*
4. *Pantoea agglomerans*
5. *Klebsiella oxytocca*
6. The 202 isolates include multiple, distinct CPE from 20 patients:
    - Three patients with *E. coli* with NDM-5 and *E. coli* with OXA-181
    - Two patients with *E. coli* with NDM-5 and *E. coli* with OXA-484
    - One patient with *E. coli* with OXA-181 and *E. coli* with NDM-5 & OXA-181
    - One patient with *E. coli* with NDM-5 and *E. coli* with OXA-244
    - One patient with ST648 *E. coli* with NDM-5 and ST8346 *E. coli* with NDM-5
    - One patient with *E. coli* with NDM-5 and *E. coli* with NDM-5 & OXA-181
    - One patient with *E. coli* with NDM-5 and *K. pneumoniae* with NDM-5
    - One patient with *E. coli* with NDM-5 and *K. pneumoniae* with NDM-5
    - One patient with *E. coli* with OXA-48 and *K. pneumoniae* with OXA-48
    - One patient with *E. coli* with NDM-5 and *K. pneumoniae* with NDM-5 & OXA-232
    - One patient with *E. coli* with NDM-5 & OXA-181 and *K. pneumoniae* with NDM-5 & OXA-181
    - One patient with *E. coli* with NDM-5 and *Citrobacter braakii* with NDM-5
    - One patient with *E. cloacae* complex with NDM-1 and *C. freundii* with NDM-1
    - One patient with *E. coli* with NDM-5, *E. coli* with OXA-181 and *E. coli* with OXA-484
    - One patient with *E. coli* with NDM-90, *E. coli* with OXA-48 and *E. cloacae* complex with OXA-181
    - One patient with ST405 *E. coli* with NDM-5, ST648 *E. coli* with NDM-5 and *E. coli* with OXA-181
    - One patient with *E. coli* with OXA-181, *E. coli* with OXA-484, *E. coli* with OXA-1181, *E. coli* with NDM-5 & OXA-1181

Eighteen isolates were identified in 2023 that contained more than one carbapenemase gene (Table 1). One isolate contained two NDM genes and OXA-232. Seventeen isolates contained two carbapenemase genes, all with an NDM gene and a gene belonging to the OXA-48 group (Table 1). Isolates with more than one carbapenemase gene are becoming more common, with nearly half of all isolates (28/52) found in New Zealand being isolated in 2022 and 2023. To date all isolates have contained an NDM gene and an OXA-48-like gene, except for three isolates likely to contain two NDM genes.

Probable place of acquisition of carbapenemase–producing Enterobacterales

Travel history was available for 143 of the 176 patients (81.2%), of which 73.4% (105/143) had been overseas. Fifty-one patients (51/143, 35.7%) were likely to have acquired their carbapenemase genes in the Indian subcontinent, 22 (15.4%) in other parts of Asia, 12 (8.4%) in the Western Pacific, and 20 in other parts of the world. (Table 2). Of the CPE likely to have been acquired overseas, 31.2% (34/109) were from patients who had been hospitalised. Patients with CPE that had been overseas but had not been hospitalised, had travelled to a wide range of regions, with the most common being the Indian subcontinent (34 patients), other parts of Asia (14) and the Western Pacific (6).

Transmission of carbapenemase–producing Enterobacterales in New Zealand

Thirty-eight patients, with a total of 38 CPE, had no history of recent overseas travel. For 25 of these isolates there was no epidemiological evidence reported that would support transmission in New Zealand. However, the remaining 13 isolates epidemiological evidence indicated transmission in New Zealand had occurred.

The first probable transmission events involved nine ST58 *E. coli* with NDM-5. These isolates were linked to a cluster in a Dunedin long term care facility, and were collected between May and July 2023. The source of the cluster was not identified.

The second probable transmission events involved *E. coli* containing OXA-48 linked to a community cluster in the Wellington region that started in August 2018 (related to a food outlet).[21,22] To the end of 2023, a total of 30 genetically related isolates that are considered part of this cluster, have been isolated from patients. Four new cases were identified in 2023, the last in June 2023.

TABLE 2: Probable place of acquisition of carbapenemase-producing Enterobacterales, 2022

Carbapenemase type and subtype	Number of isolates[1] from each probable region of acquisition							
	Indian subcontinent	New Zealand[2]	Other parts of Asia[3]	Other known[4]	Western Pacific	Overseas[5]	Not known[6]	Total
NDM	**34**	**27**	**15**	**7**	**6**	**3**	**20**	**112**
NDM-1	0	0	2	1	5	0	1	9
NDM-5	34	25	12	6	1	3	19	100
NDM-7	0	1	0	0	0	0	0	1
NDM-13	0	1	0	0	0	0	0	1
NDM-90	0	0	1	0	0	0	0	1
OXA-48-like	**22**	**5**	**10**	**9**	**3**	**3**	**10**	**62**
OXA-48	0	5	5	4	1	1	1	17
OXA-181	12	0	5	2	2	0	7	28
OXA-244	0	0	0	3	0	2	2	7
OXA-484	9	0	0	0	0	0	0	9
OXA-1181	1	0	0	0	0	0	0	1
NDM and OXA-48-like	**11**	**1**	**1**	**0**	**2**	**1**	**2**	**18**
NDM-1 and OXA-232	2	0	0	0	0	0	1	3
NDM-5 and OXA-181	6	0	0	0	2	1	0	9
NDM-5 and OXA-232	0	0	1	0	0	0	0	1
NDM-5 and OXA-484	1	0	0	0	0	0	0	1
NDM-5 and OXA-1181	1	0	0	0	0	0	0	1
NDM-5 and OXA-1205	0	1	0	0	0	0	0	1
NDM-5 and OXA-1207	0	0	0	0	0	0	1	1
NDM-1, NDM-5 and OXA-232	1	0	0	0	0	0	0	1
Other genes	**0**	**5**	**0**	**0**	**3**	**0**	**2**	**10**
IMP-4	0	1	0	0	3	0	2	6
KPC-3	0	1	0	0	0	0	0	1
OXA-23	0	3	0	0	0	0	0	3
Total	**67**	**38**	**25**	**16**	**14**	**7**	**35**	**202[1]**

Footnotes Table 2

1 Includes multiple isolates from 20 patients who had multiple distinct CPE (see Table 1, footnote 6). Twelve of these patients reported recent travel to the Indian subcontinent (with four hospitalised while there), three patients had travelled to Other parts of Asia (with one hospitalised), two patients had travelled to the Western Pacific (with one hospitalised), one patient was hospitalised in the Eastern Mediterranean, one patient had travelled to Africa, and one travelled to Europe.

2 Includes 13 isolates that were most likely acquired in New Zealand: nine *E. coli* isolates with NDM-5 and four *E. coli* with OXA-48. The likely source of the other 25 CPE from patients with no recent international travel was not determined.

3 All Asia other than the Indian subcontinent.

4 One patient with a CPE with NDM-1 who travelled to Africa, 6 patients with CPE with NDM-5 who travelled to Africa (4) or the Eastern Mediterranean (2), 4 patients with a CPE with OXA-48 who travelled to Africa (1) or Europe (3), two patients with a CPE with OXA-181 who travelled to the Eastern Mediterranean, and three patients with a CPE with OXA-244 that travelled to the Eastern Mediterranean.

5 Three patients who travelled to an unspecified country had a CPE with NDM-5 (2) or OXA-244 (1), two patients who travelled to both Europe and the Eastern Mediterranean had a CPE with OXA-48 (1) or OXA-244 (1), one patient who travelled to both the Indian subcontinent and the Americas had a CPE with NDM-5 and OXA-181, and one patient who travelled to the Western Pacific and Europe had a CPE with NDM-5.

6 Isolates from 35 patients where the travel history was not reported.

CPE phenotypic antimicrobial susceptibility testing results

Referring laboratories were asked to provide PHF Science with their susceptibility results, which are summarised in Table 3. The 46 meropenem-susceptible isolates with a carbapenemase gene contained either OXA-181 (20 isolates), OXA-48 (11 isolates), OXA-484 (5 isolates), OXA-244 (4 isolates), OXA-23 (2 isolates), IMP-4 (2 isolates), OXA-1181 (1 isolates) or NDM-5 (1 isolate). Multi-resistance, defined as resistance to three or more classes of antimicrobials, was common. However, there were exceptions, with a number of isolates with an OXA-48-like carbapenemase resistant to two or fewer of the antimicrobials tested.

Resistance genes found in CPE

Most isolates with a carbapenemase gene also had a number of other resistance genes present, including genes conferring resistance to aminoglycosides (165, 81.7%), sulphonamides (163, 80.7%), trimethoprim (157, 77.7%), tetracycline (119, 58.9%) and fluoroquinolones (111, 55.0%).

Forty-two isolates from 39 patients contained a 16S ribosomal methyl transferase (*armA* or *rmt*) gene, which confers high-level resistance to all clinically relevant aminoglycosides. Travel history was known for 31 of the 39 patients, with 27 of these reporting recent international travel. The most common region patients with a 16S ribosomal methyl transferase gene had travelled was the Indian subcontinent (21/27).

One isolate with a mobile colistin resistance gene was identified. This isolate contained the carbapenemase IMP-4 and the *mcr*9 gene. No other *mcr* genes were identified in any of the isolates.

Extended spectrum beta lactamase genes (ESBL) were found in 88 CPE, with all except one containing a CTX-M gene. The most common CTX-M subtype was CTX-M-15, found in 71 isolates.

TABLE 3: Susceptibility results for CPE in 2023, generated by diagnostic laboratories interpreted by EUCAST 2023 breakpoints

Antimicrobial	Percentage of isolates for each carbapenemase group											
	Total CPE (n=202)			MBL[1] (n=118)			NDM and OXA (n=18)			OXA-48-like (n = 62)		
	S[2]	R[2]	No. tested	S[2]	R[2]	No. tested	S[2]	R[2]	No. tested	S[2]	R[2]	No. tested
Amoxicillin-clavulanate	0.0	99.3	144	0.0	100.0	82	0.0	92.3	13	0.0	100.0	46
Cefoxitin	16.2	81.1	148	1.1	97.8	89	0.0	100.0	16	52.5	40.0	40
Ciprofloxacin	15.0	78.4	167	14.6	79.2	96	0.0	94.4	18	17.7	74.5	51
Co-trimoxazole	22.9	77.1	157	8.8	91.2	91	0.0	100.0	16	53.2	46.8	47
Ertapenem	10.9	88.1	101	1.7	96.7	60	0.0	100.0	14	38.5	61.5	26
Fosfomycin	88.6	11.4	70	83.8	16.2	37	87.5	12.5	8	95.8	4.2	24
Gentamicin	63.0	36.4	173	57.4	41.6	101	27.8	72.2	18	84.3	15.7	51
Imipenem	24.4	63.4	41	0.0	83.3	24	0.0	100.0	5	81.8	9.1	11
Meropenem[3]	27.4	69.1	168	2.9	92.2	103	0.0	100.0	17	89.1	8.7	46
Nitrofurantoin	76.6	23.4	107	92.5	7.5	67	80.0	20.0	10	44.4	55.6	27
Norfloxacin	17.9	81.0	84	18.2	80.0	55	0.0	100.0	8	15.8	84.2	19
Piperacillin-tazobactam	1.5	97.7	132	2.5	96.2	79	0.0	100.0	13	0.0	100.0	37
Trimethoprim	23.4	76.6	107	7.5	92.5	67	20.0	80.0	10	55.6	44.4	27

1 Incudes all isolates with an MBL gene only.

2 S = susceptible, R = resistant ≥ 90% Susceptible 70 - 89% Susceptible < 70% Susceptible

3 The 48 meropenem-susceptible isolates contained either OXA-181 (20), OXA-48 (12), OXA-244 (4), OXA-484 (4), NDM-5 (1), OXA-23 (2), IMP-4 (2) or OXA-1181 (1).

Multilocus sequence types identified in CPE

The 7-gene multilocus sequence type (MLST) was available for 94.4% of the *E. coli* (153/162) with acquired carbapenemase genes. A total of 53 different sequence types were found, with only nine sequence types found in five or more isolates (Table 4). For most sequence types, a single carbapenemase gene was predominant, although diversity was observed (Table 4).

Multilocus sequence types were available for 23 *K. pneumoniae* isolates. Twelve distinct sequence types were found, with the most common sequence type, ST147, found in five isolates (Table 4).

TABLE 4: Sequence types found in carbapenemase-producing Enterobacterales in 2023

Species/ sequence type	No. of isolates	Carbapenemase genes present
Escherichia coli	**162**	
ST167	14	NDM-5 (10), OXA-244 (2), NDM-5 and OXA-181 (1), NDM-5, OXA-484 (1)
ST648	14	NDM-5 (11), OXA-484 (2), OXA-1181 (1)
ST372	12	OXA-181 (12)
ST405	11	NDM-5 (8), NDM-5 and OXA-181 (1), OXA-48 (1), OXA-181 (1)
ST410	10	NDM-5 (7), OXA-484 (2), OXA-181 (1)
ST38	9	OXA-48 (3), OXA-244 (3), NDM-5 (2), OXA-181 (1)
ST58	9	NDM-5 (9)[1]
ST131	8	OXA-48 (5)[2], NDM-5 (2), OXA-484 (1)
ST361	5	NDM-5 (5)
Other ST	61	
Unknown ST	9	
Klebsiella pneumoniae	**23**	
ST147	5	NDM-5 (5)
ST16	3	NDM-5 and OXA-181 (2), OXA-181 (1)
ST395	3	NDM-1 and OXA-232 (2), NDM-1 and NDM-5 and OXA-232 (1)
ST15	2	NDM-5 (1), NDM-1 and OXA-232 (1)
ST25	2	IMP-4 (2)
ST437	2	NDM-5 and OXA-232 (1), OXA-48 (1)
Other ST	6	

1 Nine ST58 *E. coli* with NDM-5 were linked to a cluster in a Dunedin long term care facility

2 Four ST131 *E. coli* with OXA-48 were linked to a community cluster in the Wellington region

Genomic relatedness of carbapenemase-producing Enterobacterales

Genome-wide analysis of WGS data was used to investigate the genetic relatedness of CPE identified in 2023, which were compared to other CPE in the PHF Science database. These analyses provided greater resolution than 7-gene MLST and were undertaken in near-real time to detect any possible clusters of isolates in New Zealand. The cluster analyses confirmed the genomic relatedness of isolates linked to the Dunedin long term care facility as well as isolates related to the Wellington community cluster. One further possible cluster was identified that involved 12 ST372 *E. coli* with the OXA-181 carbapenemase gene from 12 patients in the wider Auckland region. Isolates were found between March 2023 and November 2023. An investigation into this outbreak was undertaken, led by Health New Zealand Te Toka Tumai Auckland, although no conclusive epidemiological links between patients were identified.

CARBAPENEMASE-PRODUCING PSEUDOMONAS SPP.

A total of 7 distinct CPP were isolated from seven patients in 2023 (Figure 2), which is similar to the number of CPP isolated in 2022 when six CPP were found.[23] All seven CPP were *P. aeruginosa*. The sample source was provided for all isolates, which were isolated from urine (3 isolates), a sterile site (1), a skin and soft tissue sample (1), an ear sample (1) and a screening sample (1). Six isolates were referred from laboratories in the Auckland region and one was referred from Canterbury. The carbapenemase genes found were: NDM-1 (4 isolates), VIM-2 (2 isolates) and IMP-1 (1 isolate). Two of the seven patients also carried a CPE. Six patients with a CPP had known travel history, of which five had recent international travel, with three being hospitalised overseas. Susceptibility data was supplied for six of the CPP, with all being resistant to carbapenems (6/6) and piperacillin-tazobactam (6/6) and 80% being resistant to fluoroquinolones (5/6) and gentamicin (5/6). The 7-gene MLST was available for five of the isolates, which were ST773 (2), ST111 (1), ST235 (1), and ST446 (1). Cluster analysis indicated that the two ST773 isolates were similar, but differed at 12 cgMLST alleles, indicating that direct transmission was unlikely to be direct; both patients reported recent international travel.

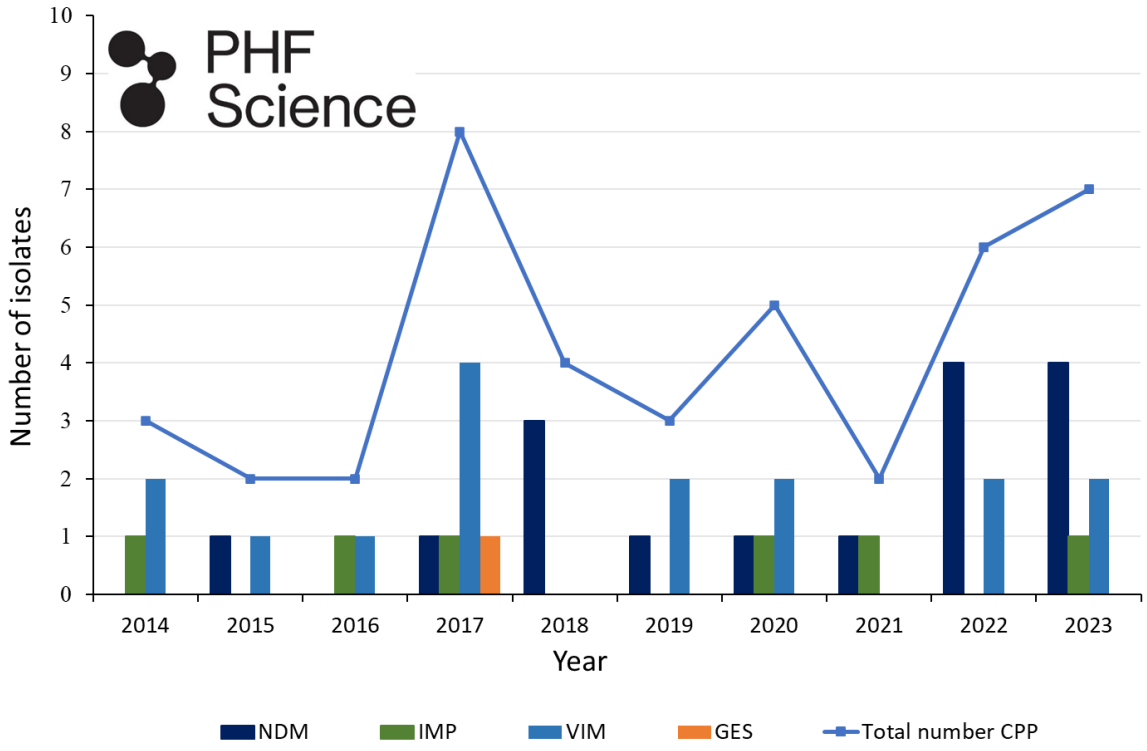

FIGURE 2: Number of carbapenemase-producing *Pseudomonas* spp. isolates identified in New Zealand, by carbapenemase class, from 2014 to 2023

CONCLUSION

Carbapenem resistance continues to be of concern in New Zealand, with numbers of CPE in 2023 double that found in 2022.[20] The increase was largely attributable to the increase in *E. coli* with acquired carbapenemase genes, with three times more found in 2023 compared to 2022.[20] By contrast the numbers of *K. pneumoniae* and *Pseudomonas* spp. with acquired carbapenemase genes remained reasonably constant. The increase in CPOs in New Zealand is likely partially attributable to the re-opening of the New Zealand border, which fully opened during 2022, following restrictions imposed to control the SARS-CoV-2 pandemic. This supports the theory that most CPO identified in New Zealand originates overseas.

The proportion of CPO likely to have been acquired in New Zealand remains low, but the numbers are increasing. Between 2019 and 2022 the number of CPE from patients with no recent travel history fluctuated between 20-22 cases annually,[20] but in 2023 38 cases were found. This change was not statistically significant, but the number of locally acquired cases needs to be monitored in the future. The increase in patients with CPE that have no recent travel history may be partially due to the limitations in the collection of travel history data. As CPO are not notifiable in New Zealand, collection and storage of travel history data is done outside the EpiSurv database used for notifiable diseases. PHF Science relies on referring laboratories to obtain travel history information from patients and forward the information. While the system for data collection is good, referral of this data is not mandatory.

There are also increasing numbers of patients with a CPO whose travel history is not available. This is likely partially due to an increase in submissions from community-based patients, as their travel history is unable to be clarified. NDM and OXA-48-like genes remain the dominant carbapenemase genes in CPO in New Zealand, although VIM genes were also common in CPP. There was an increase in CPE with multiple carbapenemase genes, with isolates containing both an NDM and an OXA-48-like gene being the most common. As expected, CPO described in this report are highly multidrug resistant, across multiple antimicrobial classes, with limited treatment options available.

Epidemiological and genomic evidence support local acquisition of CPO in some patients in 2023. This highlights the importance of ongoing, continuous surveillance to ensure clusters of related isolates are detected early in New Zealand, which is needed

to minimise spread and prevent outbreaks within healthcare, residential facilities and communities. Additionally, PHF Science must continue to receive confirmed or suspected CPO from diagnostic laboratories for further molecular characterisation, to help identify any linkages with cross transmission events. We thank the diagnostic laboratories for their ongoing contribution to this important surveillance.

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