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Summary Report

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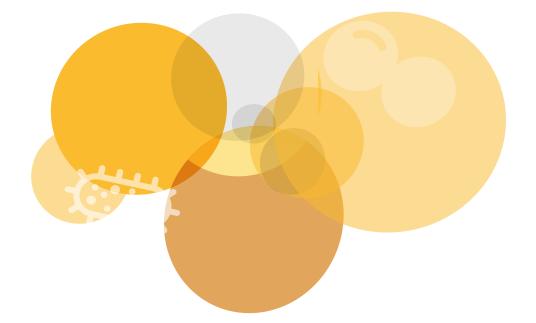
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Summary

The National Alert System for Critical Antimicrobial Resistances (CARAlert) was established by the Australian Commission on Safety and Quality in Health Care (the Commission) in March 2016 as part of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System. AURA is funded by the Australian Government Department of Health. In the second year of operation the CARAlert collects surveillance data on priority organisms with critical resistance to last-line antimicrobial agents, these reports are critical to ensure timely response by hospitals, clinicians, patients, infection control practitioners and state and territory health departments.

Critical antimicrobial resistances (CARs) are resistance mechanisms, or profiles, known not to respond effectively to last-line antimicrobial agents. This constitutes a significant threat to human health and life.

This report is the latest in a series produced by the AURA National Coordination Unit (NCU) which provide regular data updates and six-monthly detailed analyses of CARAlert data. This report includes information about isolates collected between 1 October 2017 and 31 March 2018, and the results reported into CARAlert by 30 April 2018.

Azithromycin non-susceptible *Neisseria* gonorrhoeae were the most frequently reported CAR of all CAR types (46.6%) during the reporting period, followed by carbapenemase-producing Enterobacterales (CPE) either alone (36.9%) or in combination with ribosomal methyltransferases (RMT) (2.1%).

Forty-eight percent of CARs were detected from hospitalised patients or hospital outpatients. Although the total number of CARs reported was the same as for the corresponding reporting period from October 2016 to March 2017, there was a significant increase (266%) in multidrug-resistant *Shigella* species (9 to 33; P <0.001). Shigellosis is a diarrhoeal disease caused by infection with the *Shigella* bacteria. There was a decrease (26%) in azithromycin non-susceptible (low-level resistance <256 mg/L) *N. gonorrhoeae* (339 to 249; P < 0.001). There was an increase 20% in the overall number of CPE that was not statistically significant (213 to 255). Five *N. gonorrhoeae* strains with high-level azithromycin non-susceptibility (MIC > 256 mg/L) were confirmed from two states; New South Wales (3, February 2018), and Victoria (2, March 2018). Since 2014 there have been sporadic reports of *N. gonorrhoeae* strains with high-level resistance to azithromycin reported in Australia.¹

In addition there were two *N. gonorrhoeae* strains reported that were resistant to ceftriaxone and azithromycin non-susceptible (high-level resistance, MIC > 256 mg/L) from two patients residing in Queensland.² These patients have received appropriate treatment for the infection. The detection of these strains is of concern because of the potential public health implications of an outbreak of extensively drugresistant *N. gonorrhoeae*. The findings highlight the importance of sexually transmitted infection prevention and control programs.

CPE reports continue to be dominated by those of the IMP type, found most often in the *Enterobacter cloacae* complex. The frequency of reporting of CPE highlights the importance of the implementation of the Commission's <u>Recommendations for the control of</u> <u>carbapenemase-producing Enterobacterales: a</u> guide for acute health facilities.³

The Commission continues to regularly monitor records from CARAlert, prepare summary reports and ensure regular discussion with state and territory health departments about trends and potential CAR outbreaks to inform quality improvement initiatives and policies to reduce antimicrobial resistance.

The Commission has commenced consultation with all states and territories regarding the establishment of a network for coordination of response to outbreaks of resistant organisms in Australia. CARAlert will be significant in informing this process.



Background

The Australian Commission on Safety and Quality in Health Care (the Commission) established the National Alert System for Critical Antimicrobial Resistances (CARAlert) in March 2016 as part of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System.

Critical antimicrobial resistances (CARs) are defined as resistance mechanisms, or profiles, known to be a serious threat to the effectiveness of last-line antimicrobial agents. They can result in significant morbidity and mortality in healthcare facilities, and in the community. The CARs reported under CARAlert are listed in Table 1. The CARs were drawn from the list of high-priority organisms and antimicrobials which are the focus of the AURA Surveillance System.⁴

The Commission is currently reviewing the resistances and species reported to CARAlert in conjunction with relevant experts and the states and territories.

The CARAlert system is based on the following routine processes used by pathology laboratories for identifying and confirming potential CARs:

- Collection and routine testing the isolate is collected from the patient and sent to the originating laboratory for routine testing
- Confirmation if the originating laboratory suspects that the isolate is a CAR, it sends the isolate to a confirming laboratory that has the capacity to confirm the CAR
- Submission to the CARAlert system the confirming laboratory advises the originating laboratory of the result of the test, and the originating laboratory reports back to the health service that cared for the patient from whom the specimen was collected; the confirming laboratory then submits the details of the resistance and organism into the secure CARAlert web portal.

Table 1 List of critical antimicrobial resistances

Species	Critical Resistance
Enterobacterales	Carbapenemase-producing, and/or ribosomal methyltransferase-producing
Enterococcus species	Linezolid non-susceptible
Mycobacterium tuberculosis	Multidrug-resistant - resistant to at least rifampicin and isoniazid
Neisseria gonorrhoeae	Ceftriaxone or azithromycin non-susceptible
Salmonella species	Ceftriaxone non-susceptible
Shigella species	Multidrug-resistant
Staphylococcus aureus	Vancomycin, linezolid or daptomycin non-susceptible
Streptococcus pyogenes	Penicillin reduced susceptibility

Results

This six-month report provides details on confirmed CARs collected between 1 October 2017 and 31 March 2018 and the results reported into CARAIert by 30 April 2018. It complements the <u>CARAIert updates and reports</u> that are published regularly on the Commission's website.

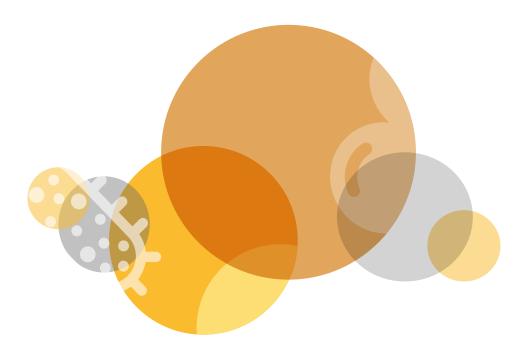
As there is a time-lag in confirmation for some isolates, the cut-off date for data included in Commission updates and reports is four weeks after the end of each reporting period. The data in each update and report are based on the date that the isolate with a confirmed CAR was collected.

Critical antimicrobial resistances reported by state and territory

Between 1 October 2017 and 31 March 2018, 653 results from 58 originating laboratories across Australia were entered in the CARAlert system (Table 2). Azithromycin non-susceptible *Neisseria gonorrhoeae* were the most frequently reported CAR of all CAR types (46.6%), followed by carbapenemase-producing Enterobacterales (CPE) either alone (36.9%) or in combination with ribosomal methyltransferases (RMT) (2.1%). No vancomycin non-susceptible *Staphylococcus aureus* were reported during this reporting period.

The majority of CARs continue to be reported from New South Wales (32%), Victoria (34%) and Queensland (21%) – the three most populous states. CARs were the lowest in Tasmania (5), the Northern Territory (4), and South Australia (1); with only 1.5% (10/653) of all CARs reported from these states and territories. Five reports were from overseas residents; two CPE, two CPE+RMT, and one multidrug-resistant *Mycobacterium tuberculosis*.

Although the total number of CARs reported was the same as for the corresponding reporting period last year, there was a significant increase of 266% in multidrug-resistant *Shigella* species (9 to 33; P <0.001) and a decrease of 26% in azithromycin non-susceptible (low-level resistance [LLR] <256 mg/L) *N. gonorrhoeae* (339 to 249; P < 0.001). There was an increase of 20% in the overall number of CPE that was not statistically significant (213 to 255).



Number of critical antimicrobial resistance isolates, by state and territory, 1 October 2017 to 31 March 2018 Table 2

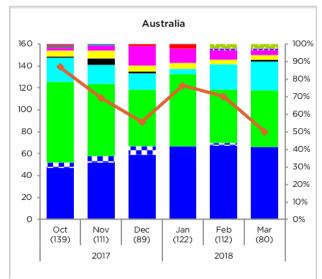
Critical antimicrobial resistance	NSW	Vic	QId	SA	WA	Tas	Łz	ACT	SO	Unk	17-Q4 18-Q1	2018 YTD	16-Q4 17-Q1	2017	Trend ⁺ Apr-17 Mar-18
Azithromycin non-susceptible (LLR < 256 mg/L) <i>Neisseria gonorrhoeae</i>	103	82	54	1	7	0	-	1	0	0	249	110	339	730	
Carbapenemase-producing Enterobacterales	71	67	70	0	18	2	М	œ	5	0	241	131	207	528	\langle
Daptomycin non-susceptible Staphylococcus aureus	11	28	12	0	21	0	0	0	0	0	72	33	59	119	2
Multidrug-resistant <i>Shigella</i> species	7	19	м	0	7	0	0	4	0	н	33	18	თ	27	\leq
Ceftriaxone non-susceptible Salmonella species	7	14	4	0	н	-	0	0	0	0	22	6	10	37	Z
Carbapenemase and ribosomal methyltransferase- producing Enterobacterales	7	м	н	0	-	0	0	0	7	0	14	5	9	33	5
Ribosomal methyltransferase-producing Enterobacterales	7	м	0	0	0	-	0	0	0	H	7	Н	თ	22	$\sum_{i=1}^{n}$
Azithromycin non-susceptible (HLR > 256 mg/L) <i>Neisseria gonorrhoeae</i>	М	7	0	0	0	0	0	0	0	0	ы	Ŋ	н	4	
Linezolid non-susceptible Enterococcus species	4	Н	0	0	0	0	0	0	0	0	Ŋ	м	0	Ŋ	
Ceftriaxone non-susceptible and azithromycin non- susceptible (HLR > 256 mg/L) <i>Neisseria gonorrhoeae</i>	0	0	2	0	0	0	0	0	0	0	2	2	0	0	
Multidrug-resistant Mycobacterium tuberculosis	0	0	0	0	0	Ч	0	0	Ч	0	7	0	6	6	
Linezolid non-susceptible Staphylococcus aureus	0	0	Ч	0	0	0	0	0	0	0	Ч	0	ю	Ч	
	210	219	147	1	50	Ŋ	4	10	ы	7	653	314	652	1,515	
HLR = high-level resistance; LLR = low-level resistance; OS = overseas;	S = ove	10	Unk = unknown; YTD	known;	ΥTD =	= year to date	date							-	

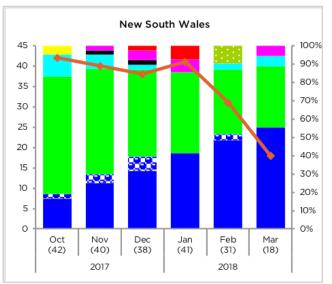
⁺ Trend Apr-17 Mar-18 = 12-month trend, 1 April 2017 to 31 March 2018

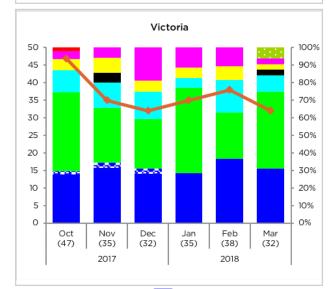
Critical antimicrobial resistances reported by species by month

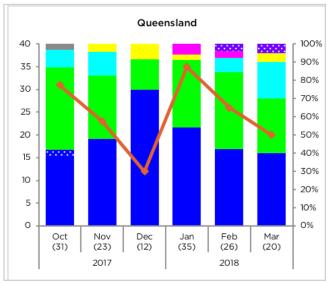
The number and distribution of CARs reported nationally, and by state and territory, from 1 October 2017 to 31 March 2018, is shown in Figure 1. There was an average of 109 entries per month (range 80–139), with notable state and territory variation

Figure 1: Critical antimicrobial resistances, number and distribution reported nationally, by state and territory, and by month, 1 October 2017 to 31 March 2018









Carbapenemase-producing Enterobacterales

Carbapenemase and ribosomal methyltransferase-producing Enterobacterales

Azithromycin non-susceptible (LLR < 256 mg/L) Neisseria gonorrhoeae

Daptomycin non-susceptible Staphylococcus aureus

Ribosomal methyltransferase-producing Enterobacterales

Ceftriaxone non-susceptible Salmonella species

Multidrug-resistant Shigella species

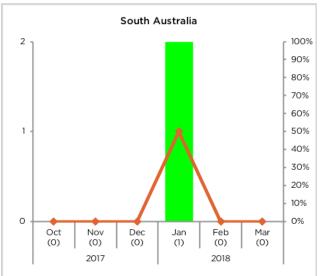
Multidrug-resistant Mycobacterium tuberculosis

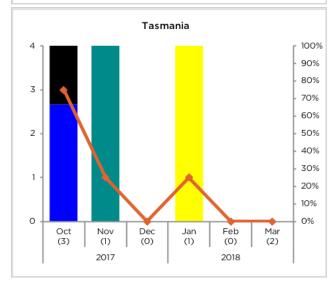
Linezolid non-susceptible Enterococcus species

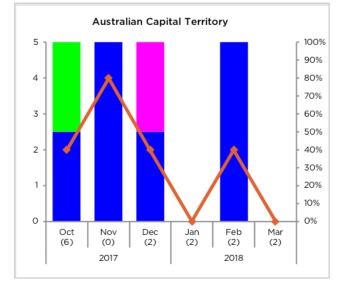
Azithromycin non-susceptible (HLR > 256 mg/L) Neisseria gonorrhoeae

Linezolid non-susceptible Staphylococcus aureus

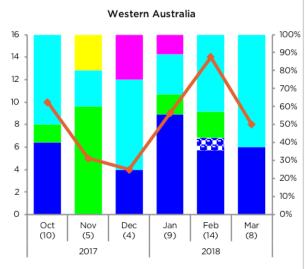
Ceftriaxone non-susceptible and azithromycin non-susceptible Neisseria gonorrhoeae

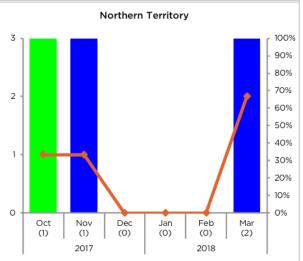












- Carbapenemase and ribosomal methyltransferase-producing Enterobacterales
- Azithromycin non-susceptible (LLR < 256 mg/L) Neisseria gonorrhoeae
- Daptomycin non-susceptible Staphylococcus aureus
- Ribosomal methyltransferase-producing Enterobacterales
- Ceftriaxone non-susceptible Salmonella species
- Multidrug-resistant Shigella species
- Multidrug-resistant Mycobacterium tuberculosis

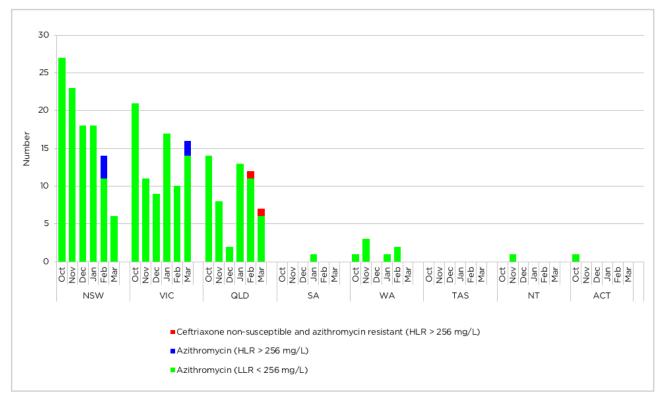
Results

Nationally, azithromycin non-susceptible *N. gonorrhoeae* were the most frequent CAR reported for October and November 2017; from December 2017 CPE dominated.

Reports of multidrug-resistant *Shigella* species peaked in December 2017 and January 2018, and now appear to be declining.

Daptomycin non-susceptible *S. aureus* were reported from four states/territories, with 39% (28/72) from Victoria, and 29% (21/72) from Western Australia. There was a notable decrease in the number of reports of azithromycin non-susceptible *N. gonorrhoeae* originating from New South Wales (Figure 2). Five strains with high-level azithromycin non-susceptibility (MIC > 256 mg/L) were confirmed from two states; New South Wales (3, February 2018), and Victoria (2, March 2018). Two *N. gonorrhoeae* that were both ceftriaxone non-susceptible and azithromycin non-susceptible (high-level resistance, MIC > 256 mg/L) were reported from two patients residing in Queensland. Both patients have received appropriate treatment for their infection.

Figure 2: Neisseria gonorrhoeae, number reported by state and territory, and month of collection*, 1 October 2017 to 31 March 2018

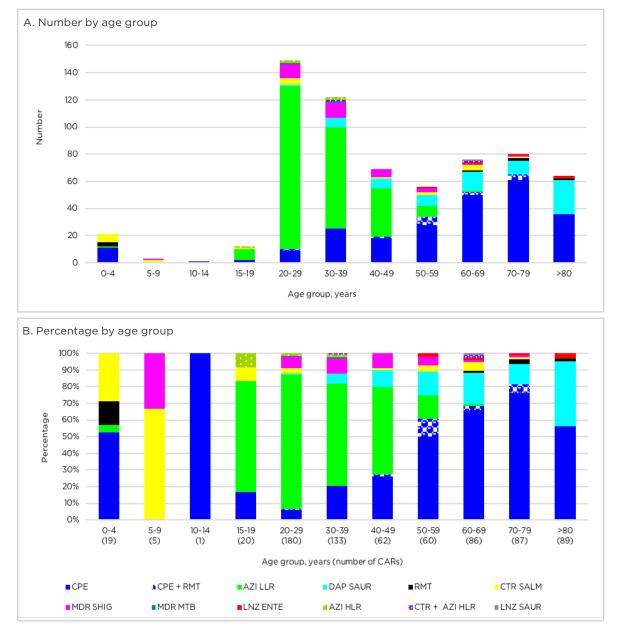


* Where state and territory of residence is unknown, the state of the originating laboratory has been assigned

Critical antimicrobial resistances by age group

CARs were isolated from patients of all ages, from birth to those aged greater than 80 years, with a median age of 40–49 years (Figure 3). Sixty per cent (153/255) of CPE were from people aged 60 years and older. Azithromycin non-susceptible *N. gonorrhoeae* were the predominant CAR reported among the age groups 15–19 years, 20–29 years, 30–39 years and 40–49 years. Only 3.8% (25/653) of all CARs were reported in children aged less than 15 years; CPE (44%) and ceftriaxone non-susceptible *Salmonella* species (32%) were common in this age group. No trends have been observed in the age distribution since the commencement of the program.





AZI LLR = azithromycin non-susceptible, low-level resistance (LLR, MIC < 256 mg/L) *Neisseria gonorrhoeae*; AZI HLR = azithromycin non-susceptible, high-level resistance (HLR, MIC > 256 mg/L) *Neisseria gonorrhoeae*; CPE = carbapenemase-producing Enterobacterales; CPE+RMT = carbapenemase- and ribosomal methyltransferase-producing Enterobacterales; CTR + AZI HLR = ceftriaxone non-susceptible and azithromycin non-susceptible, high-level resistance (HLR, MIC > 256 mg/L) *Neisseria gonorrhoeae*; CTR SALM = ceftriaxone non-susceptible *Salmonella* species; DAP SAUR = daptomycin non-susceptible *Staphylococcus aureus*; LNZ ENTE = linezolid non-susceptible *Enterococcus* species; LNZ SAUR = linezolid non-susceptible *Staphylococcus aureus*; MDR MTB = multidrug-resistant *Mycobacterium tuberculosis*; MDR SHIG = multidrug-resistant *Shigella* species; RMT = ribosomal methyltransferase-producing Enterobacterales

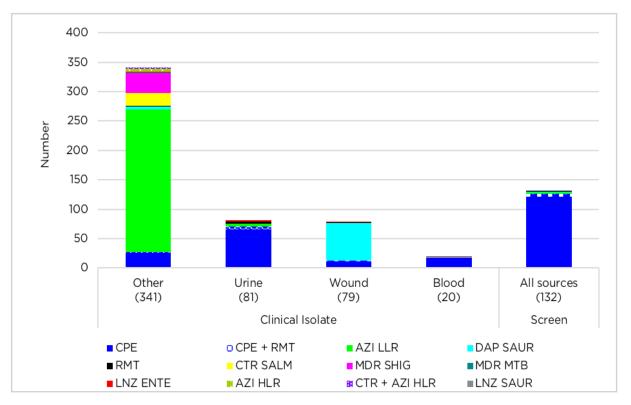
Critical antimicrobial resistances by specimen type

Eighty per cent of all CARs were from clinical specimens (specimens collected for diagnostic purposes, rather than for screening). These include urine, wound, blood and other (such as genital or respiratory) specimens (Figure 4).

Fifty-one per cent (129/255) of CPE isolates were from clinical specimens; 55% (71/129) of these were from urine, and 14% (18/129) from blood cultures.

Urine is an important specimen for certain CARs such as CPE, and the urinary tract is a common site of infection. The only other CARs reported from blood cultures were one daptomycin non-susceptible *S. aureus* and one linezolid non-susceptible *Enterococcus faecium*.

Figure 4: Critical antimicrobial resistances, number reported by specimen type, 1 October 2017 to 31 March 2018



Other specimen type: not urine, wound, or blood (for example, genital, faecal, respiratory)

AZI LLR = azithromycin non-susceptible, low-level resistance (LLR, MIC < 256 mg/L) *Neisseria gonorrhoeae*; AZI HLR = azithromycin non-susceptible, high-level resistance (HLR, MIC > 256 mg/L) *Neisseria gonorrhoeae*; CPE = carbapenemase-producing Enterobacterales; CPE+RMT = carbapenemase- and ribosomal methyltransferaseproducing Enterobacterales; CTR + AZI HLR = ceftriaxone non-susceptible and azithromycin non-susceptible, high-level resistance (HLR, MIC > 256 mg/L) *Neisseria gonorrhoeae*; CTR SALM = ceftriaxone non-susceptible *Salmonella* species; DAP SAUR = daptomycin non-susceptible *Staphylococcus aureus*; LNZ ENTE = linezolid non-susceptible *Enterococcus* species; LNZ SAUR = linezolid non-susceptible *Staphylococcus aureus*; MDR MTB = multidrug-resistant *Mycobacterium tuberculosis*; MDR SHIG = multidrug-resistant *Shigella* species; RMT = ribosomal methyltransferase-producing Enterobacterales

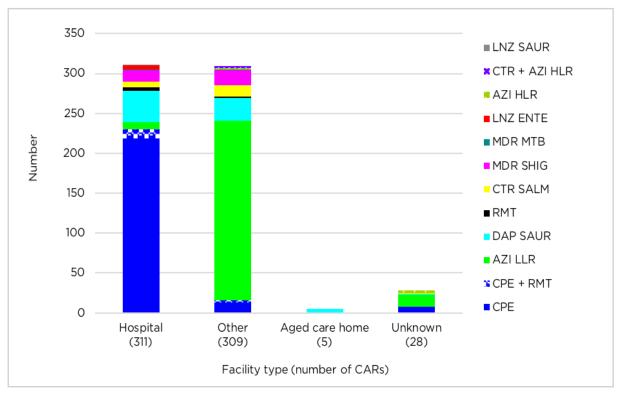
Critical antimicrobial resistances by facility type

CARs were detected in hospitalised patients or hospital outpatients (48%, 311/653), in the community (47%, 309/653), and in aged care home residents (1% 5/653) (Figure 5).

Seventy-four percent (230/311) of the CARs detected in hospitalised patients were CPE; while in aged care homes, daptomycin non-susceptible *S. aureus* were dominant (4 of 5).

Facility type for azithromycin non-susceptible *N. gonorrhoeae* was difficult to obtain as most isolates are referred to a public health laboratory for confirmation, and as such may reflect the facility from which the isolate was sent rather than the facility that the patient attended.

Figure 5: Critical antimicrobial resistances, number reported by facility type, 1 October 2017 to 31 March 2018



Other: Community (non-hospital and non-aged care home)

AZI LLR = azithromycin non-susceptible, low-level resistance (LLR, MIC < 256 mg/L) *Neisseria gonorrhoeae*; AZI HLR = azithromycin non-susceptible, high-level resistance (HLR, MIC > 256 mg/L) *Neisseria gonorrhoeae*; CPE = carbapenemase-producing Enterobacterales; CPE+RMT = carbapenemase- and ribosomal methyltransferase-producing Enterobacterales; CTR + AZI HLR = ceftriaxone non-susceptible and azithromycin non-susceptible, high-level resistance (HLR, MIC > 256 mg/L) *Neisseria gonorrhoeae*; CTR SALM = ceftriaxone non-susceptible *Salmonella* species; DAP SAUR = daptomycin non-susceptible *Staphylococcus aureus*; LNZ ENTE = linezolid non-susceptible *Enterococcus* species; LNZ SAUR = linezolid non-susceptible *Staphylococcus aureus*; MDR MTB = multidrug-resistant *Mycobacterium tuberculosis*; MDR SHIG = multidrug-resistant *Shigella* species; RMT = ribosomal methyltransferase-producing Enterobacterales

Carbapenemase-producing Enterobacterales type by state and territory

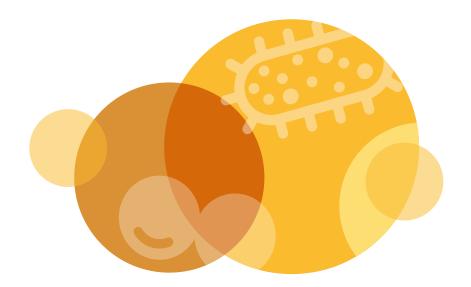
Eighty per cent of all CARs were from clinical Carbapenemase-producing Enterobacterales were reported from all states and territories reported except South Australia. Six different carbapenemase types (IMP, OXA-48-like, NDM, KPC, VIM, and IMI) were reported throughout Australia. Three carbapenemase types – IMP (56%, 144/255), NDM (22%, 56/255), and OXA-48-like (13%, 34/255) alone – accounted for 92% of all Enterobacterales with a confirmed carbapenemase. Nine Enterobacterales had multiple types (NDM+OXA-48-like [6]; IMP+KPC [1]; IMP+OXA-48-like [1], NDM+KPC [1]). Eight of nine KPC reported were from Victoria; with four from one institution.

Regional differences in the carbapenemase types reported are shown in Figure 6. IMP type carbapenemases comprised the majority of CPE in Queensland (82%, 58/71), New South Wales (63%, 49/78), and the Australian Capital Territory (75%, 6/8). All the strains that were genetically sequenced in this period (54%, 78/144) were $bla_{\rm IMP-4}$.

There was a cluster of IMP-producing Enterobacterales detected from late December 2017 to January 2018 among the age group 0-4 years in one institution in New South Wales. Six of seven isolates were *K. pneumoniae*.

NDM types were found in all states and territories except Tasmania. NDM types contributed to 36% (25/70) of all types in Victoria, 17% (13/78) in New South Wales, and 16% (3/19) in Western Australia. NDM+OXA-48-like (6/63) and NDM+KPC (n=1/63), were reported. Three different NDM genes were found in the strains sequenced to date: $bla_{\rm NDM-5}$ (70%, 19/27), $bla_{\rm NDM-1}$ (26%, 7/27), and $bla_{\rm NDM-7}$ (4%, 1/27).

Ribosomal methyltransferases were often detected among isolates containing NDM types (19%, 12/63; *rmtB* [6], *rmtC* [4], *armA* [1] and *rmtB+rmtC* [1]).



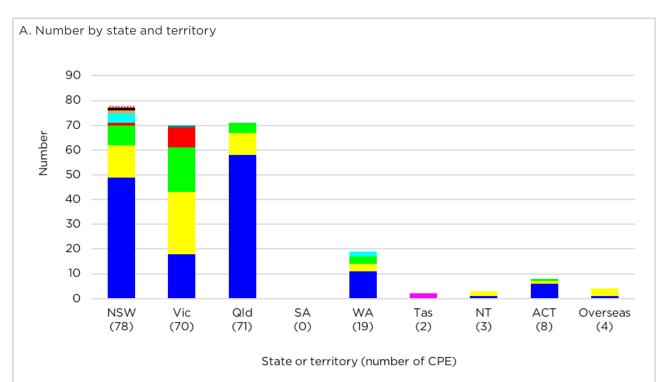
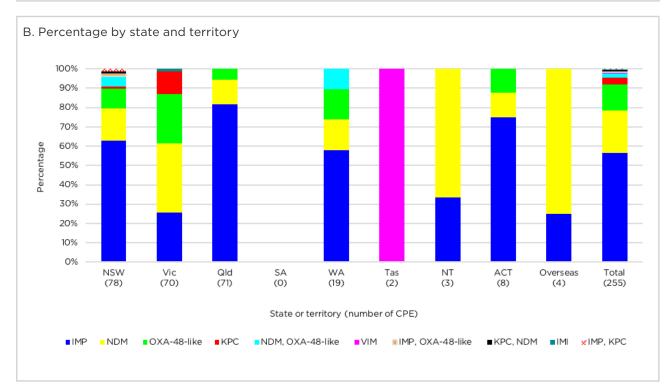


Figure 6: Carbapenemase-producing Enterobacterales*, by carbapenemase type, number (A) and percentage (B) reported by state and territory, 1 October 2017 to 31 March 2018



* Carbapenemase-producing Enterobacterales (n = 241), carbapenemase- and ribosomal methyltransferase-producing Enterobacterales (n = 14)

The distribution of carbapenemase types by state and territory and month of confirmation is shown in Figure 7. The clonal outbreak of an OXA-48 producing *E. coli* noted previously in Queensland has subsided. The twelve-month trend data for the top four carbapenemase types is shown Figure 8.

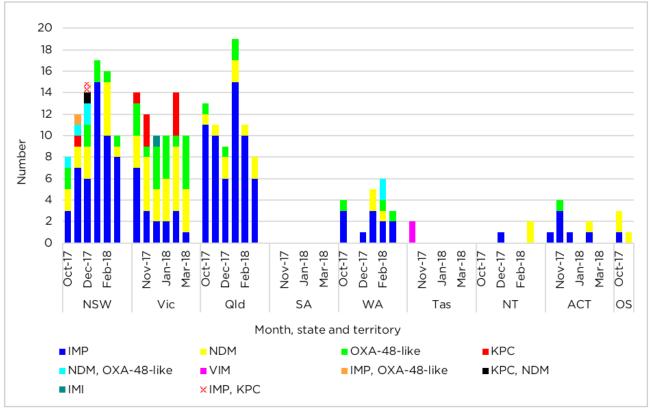


Figure 7: Carbapenemase types, number reported by month and state and territory, 1 October 2017 to 31 March 2018

OS = overseas; UNK = unknown

Figure 8: Carbapenemase types, number reported by month and state and territory, 1 October 2017 to 31 March 2018

Туре	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
IMP	~~	m	$\sim\sim$					\	\sim
OXA-48-like			\bigwedge						$\bigwedge_{}$
NDM	~~~~^	~~~	\sim		~~~		~		
КРС		M				-			\mathcal{M}

Line graphs for the period 1 April 2017 to 31 March 2018, for each type, with significant (P < 0.01) upward trends (χ^2 for trend) shaded red, and significant downward trends shaded green

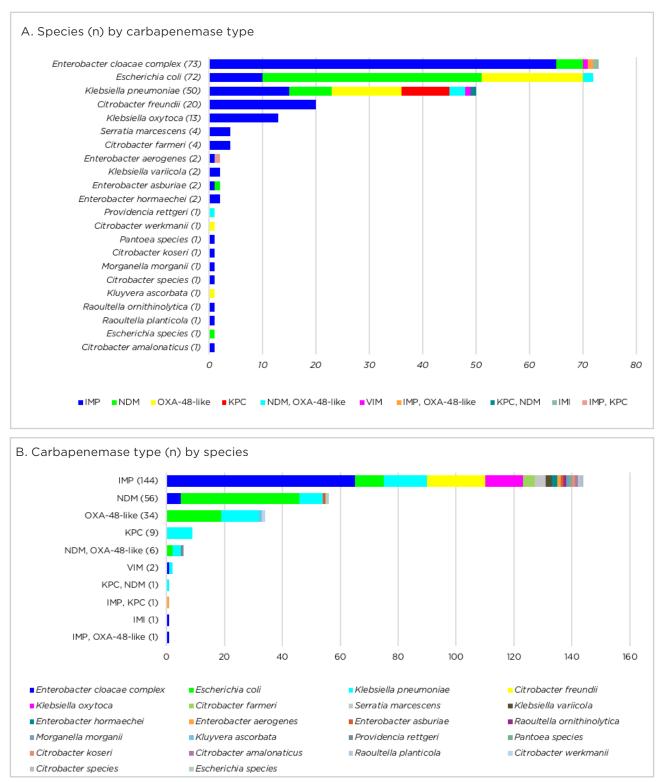
Carbapenemase-producing Enterobacterales by species and carbapenemase type

Carbapenemases were found in 22 species of Enterobacterales representing ten genera (*Citrobacter, Enterobacter, Escherichia, Klebsiella, Kluyveria, Morganella, Pantoea, Providencia, Raoultella, Serratia*). *E. cloacae* complex (30%, 77/255) and *E. coli* (28%, 72/255) contributed to 58% all species (Figure 9).

IMP-types were found in 18 different species and accounted for 57.3% (146/255) of all carbapenemases. *E. cloacae* complex accounted for 47% (69/146) of all IMP types. NDM-types were found in 24.7% (63/255) of all CPE, mainly in *E. coli* (68%, 43/63). OXA-48-like types, when detected alone, were found in mainly in *E. coli* (56%, 19/34) and *K. pneumoniae* (38%, 13/34). Eight of nine KPC were found in *K. pneumoniae* in Victoria. One *E. cloacae* complex isolate harbouring both IMP and KPC was detected from a patient residing in New South Wales.



Figure 9: Carbapenemase-producing Enterobacterales*, number reported by (A) species and (B) carbapenemase type, 1 October 2017 to 31 March 2018



* Carbapenemase-producing Enterobacterales (n = 241), carbapenemase- and ribosomal methyltransferase-producing Enterobacterales (n = 14)

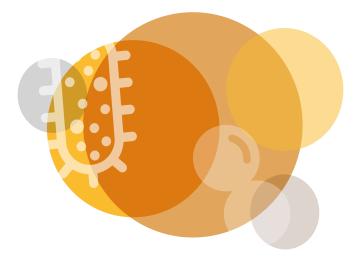
Other Critical Antimicrobial Resistance types

Ribosomal methyltransferases were detected in 21 Enterobacterales, across six different species; 67% (14/21) of these isolates also harboured a carbapenemase. Four ribosomal methyltransferase genes were found: *rmtB* (38%; 8/21); *rmtC* (24%, 5/21), *armA* (24%; 5/21), and *rmtF* (10%; 2/21); one isolate contained both *rmtB* + *rmtC*.

There were 33 reports of multidrug-resistant *Shigella* species from patients residing in Victoria (19), New South Wales (7), Queensland (3), Western Australia (1), and the Australian Capital Territory (1). The majority (79%, 26/33) were collected in the three month period December 2017-February 2018; 54% (14/26) were from patients residing in Victoria.

Twenty-two ceftriaxone non-susceptible *Salmonella* species were confirmed from Victoria (14), Queensland (4), New South Wales (2), and one each from Western Australia and Tasmania. Twelve had plasmid-borne *ampC* genes, either alone (11) or with an ESBL (1); and 10 had ESBLs alone. Seven (32%, 7/22) were isolated from hospitalised patients.

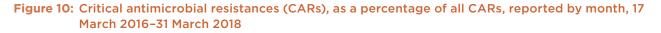
Five linezolid non-susceptible *Enterococcus* species were reported, four were *E. faecium*, and one *E. faecalis*.

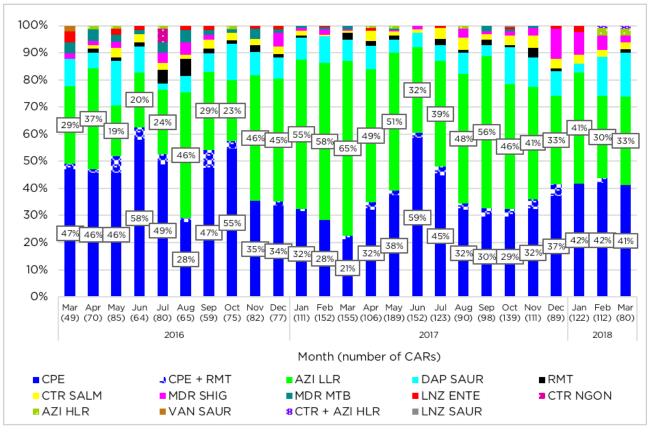


Trends since March 2016

The proportion of CARs associated with priority organisms since 17 March 2016 is shown in Figure 10. The number of CARs reported by species and month is shown in Figure 11. The number and proportion reported nationally, and by state and territory is shown in Figure 12.

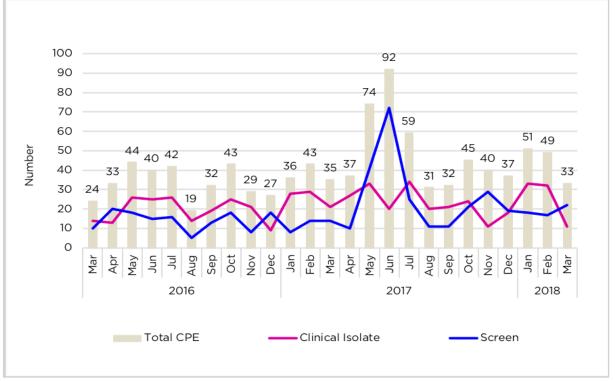
The fluctuations in reporting of CARs, particularly CPE and azithromycin non-susceptible *N. gonorrhoeae*, and state and territory variations have already been noted.





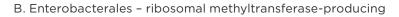
AZI LLR = azithromycin non-susceptible, low-level resistance (LLR, MIC < 256 mg/L) *Neisseria gonorrhoeae*; AZI HLR = azithromycin non-susceptible, high-level resistance (HLR, MIC > 256 mg/L) *Neisseria gonorrhoeae*; CPE = carbapenemase-producing Enterobacterales; CPE+RMT = carbapenemase- and ribosomal methyltransferaseproducing Enterobacterales; CTR + AZI HLR = ceftriaxone non-susceptible and azithromycin non-susceptible, highlevel resistance (HLR, MIC > 256 mg/L) *Neisseria gonorrhoeae*; CTR NGON = ceftriaxone non-susceptible *Neisseria gonorrhoeae*; CTR SALM = ceftriaxone non-susceptible *Salmonella* species; LNZ ENTE = linezolid non-susceptible *Enterococcus* species; LNZ SAUR = linezolid non-susceptible *Staphylococcus aureus*; DAP SAUR = daptomycin nonsusceptible *Staphylococcus aureus*; VAN SAUR = vancomycin non-susceptible *Staphylococcus aureus*; MDR MTB = multidrug-resistant *Mycobacterium tuberculosis*; MDR SHIG = multidrug-resistant *Shigella* species; RMT = ribosomal methyltransferase-producing Enterobacterales

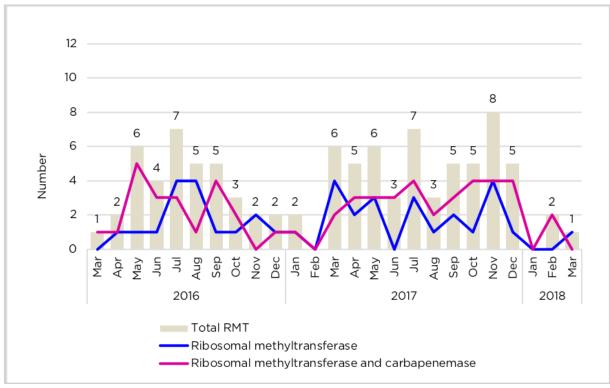
Figure 11: Critical antimicrobial resistances, number reported by species and month, 17 March 2016–31 March 2018



A. Enterobacterales - carbapenemase-producing

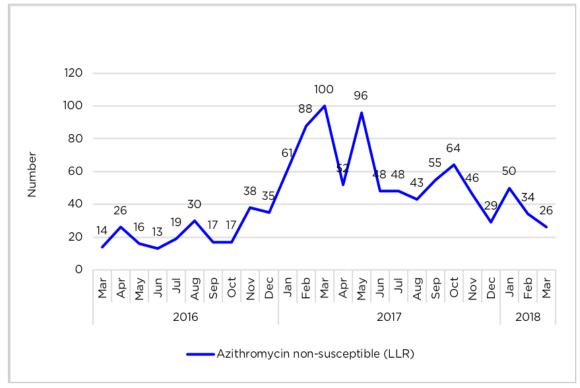
CPE = carbapenemase-producing-Enterobacterales





RMT = ribosomal methyltransferase-producing Enterobacterales

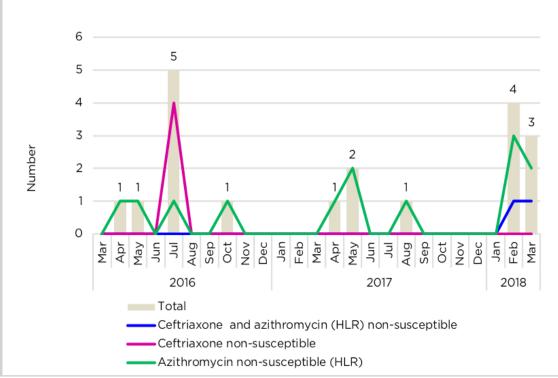
Figure 11 (continued): Critical antimicrobial resistances, number reported by species and month, 17 March 2016–31 March 2018



C. Neisseria gonorrhoeae - azithromycin non-susceptible (low level resistance)

LLR = low-level resistance

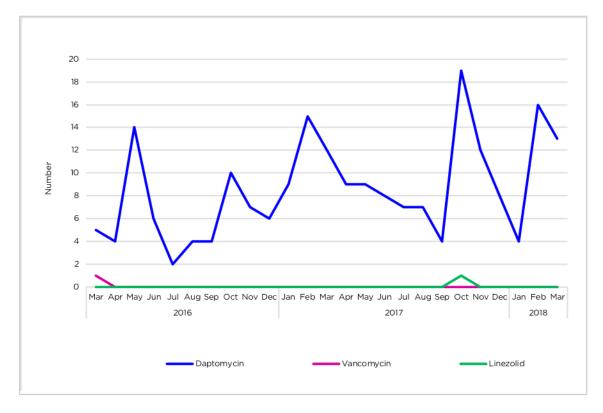
D. *Neisseria gonorrhoeae* - azithromycin non-susceptible (high level resistance) and/or ceftriaxone non-susceptible



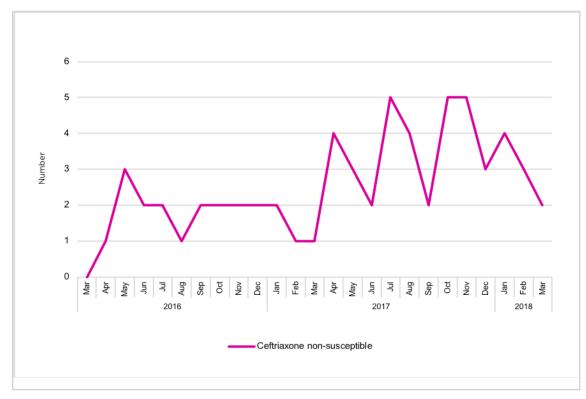
HLR = high-level resistance



E. Staphylococcus aureus

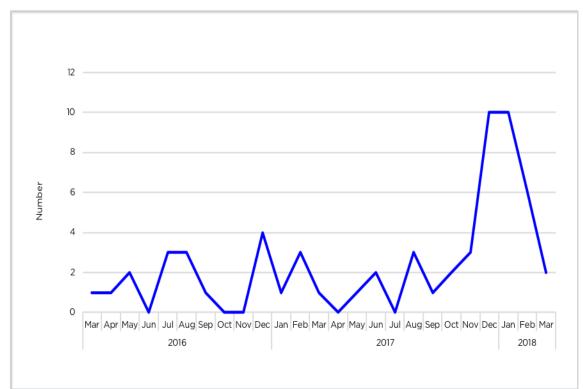


F. Salmonella species

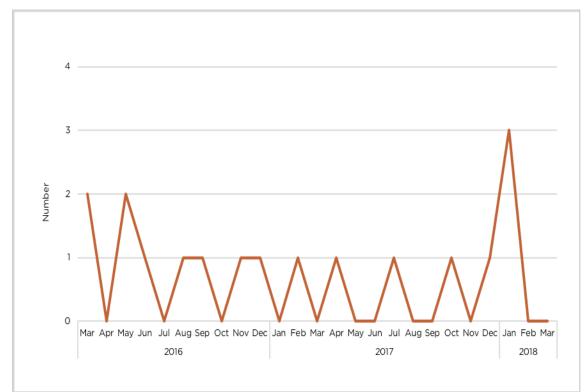




G. Shigella species

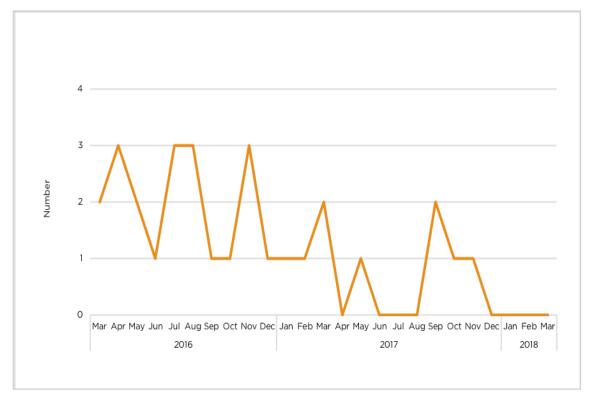


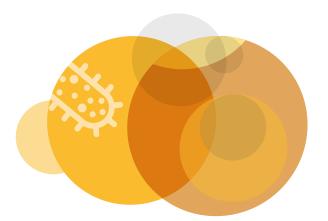
H. Enterococcus species

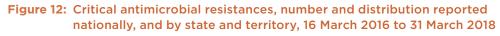


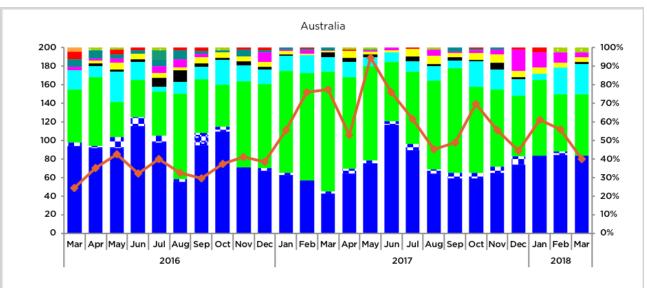


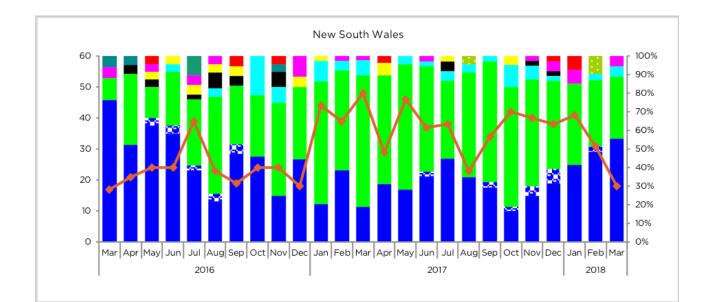
I. Mycobacterium tuberculosis











Carbapenemase and ribosomal methyltransferase-producing Enterobacterales

Azithromycin non-susceptible (LLR < 256 mg/L) Neisseria gonorrhoeae

Daptomycin non-susceptible Staphylococcus aureus

Ribosomal methyltransferase-producing Enterobacterales

Ceftriaxone non-susceptible Salmonella species

- Multidrug-resistant Shigella species
- Multidrug-resistant Mycobacterium tuberculosis
- Linezolid non-susceptible Enterococcus species
- Ceftriaxone non-susceptible Neisseria gonorrhoeae

Azithromycin non-susceptible (HLR > 256 mg/L) Neisseria gonorrhoeae

- Vancomycin non-susceptible Staphylococcus aureus
- Linezolid non-susceptible Staphylococcus aureus

Ceftriaxone non-susceptible and azithromycin non-susceptible Neisseria gonorrhoeae

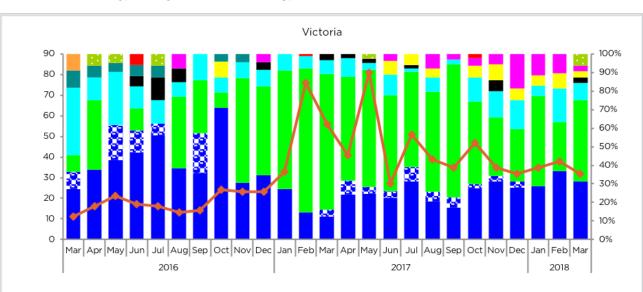
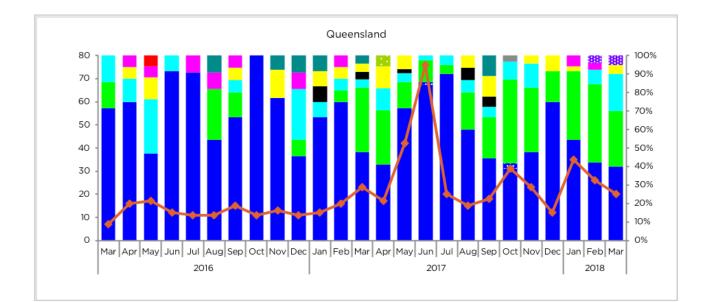


Figure 12 (continued): Critical antimicrobial resistances, number and distribution reported nationally, and by state and territory, 16 March 2016 to 31 March 2018





Carbapenemase and ribosomal methyltransferase-producing Enterobacterales

Azithromycin non-susceptible (LLR < 256 mg/L) Neisseria gonorrhoeae

Daptomycin non-susceptible Staphylococcus aureus

Ribosomal methyltransferase-producing Enterobacterales

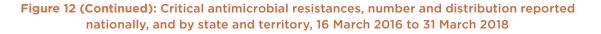
- Ceftriaxone non-susceptible Salmonella species
- Multidrug-resistant Shigella species
- Multidrug-resistant Mycobacterium tuberculosis

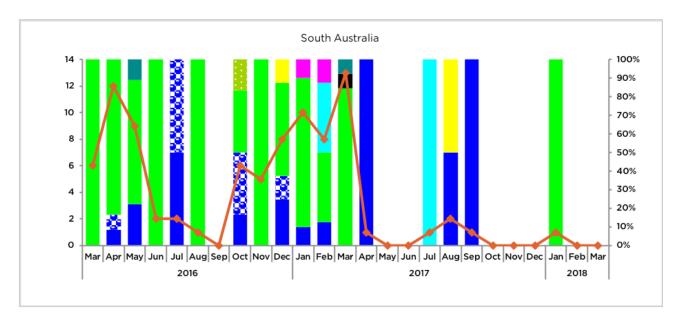
Linezolid non-susceptible Enterococcus species

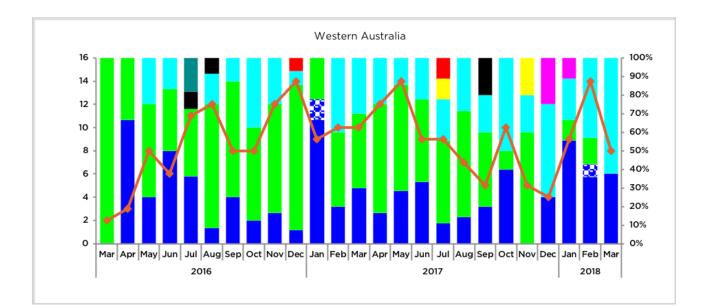
Azithromycin non-susceptible (HLR > 256 mg/L) Neisseria gonorrhoeae

- Vancomycin non-susceptible Staphylococcus aureus
- Linezolid non-susceptible Staphylococcus aureus

Ceftriaxone non-susceptible and azithromycin non-susceptible Neisseria gonorrhoeae







Carbapenemase and ribosomal methyltransferase-producing Enterobacterales

Azithromycin non-susceptible (LLR < 256 mg/L) Neisseria gonorrhoeae

Daptomycin non-susceptible Staphylococcus aureus

Ribosomal methyltransferase-producing Enterobacterales

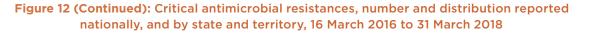
Ceftriaxone non-susceptible Salmonella species

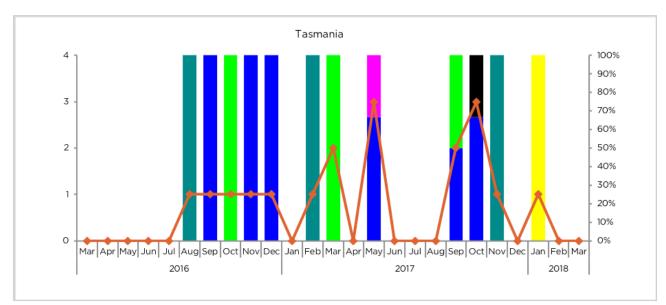
Multidrug-resistant Shigella species

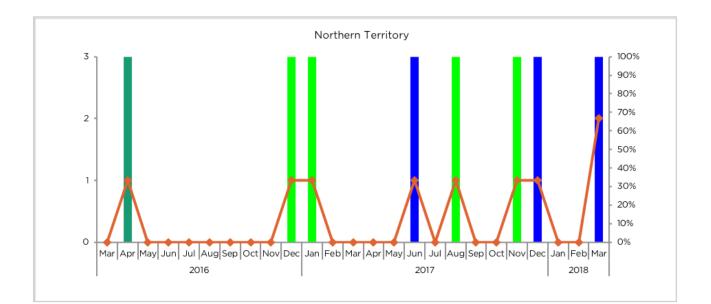
Multidrug-resistant Mycobacterium tuberculosis

Linezolid non-susceptible Enterococcus species

Azithromycin non-susceptible (HLR > 256 mg/L) Neisseria gonorrhoeae







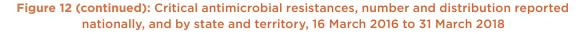
Azithromycin non-susceptible (LLR < 256 mg/L) Neisseria gonorrhoeae

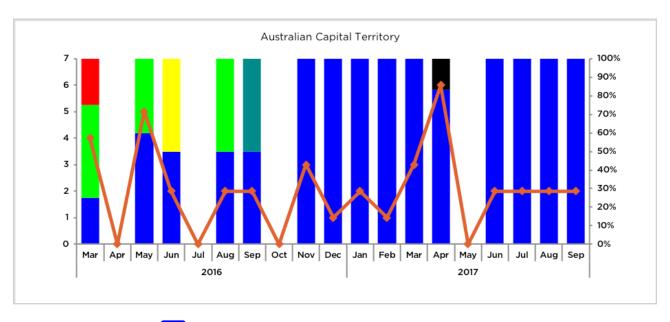
Ribosomal methyltransferase-producing Enterobacterales

Ceftriaxone non-susceptible Salmonella species

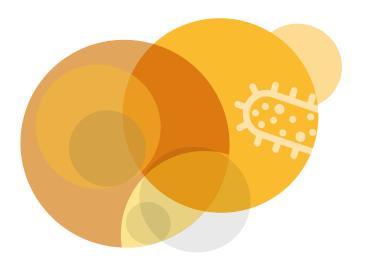
Multidrug-resistant Shigella species

Multidrug-resistant Mycobacterium tuberculosis





- Azithromycin non-susceptible (LLR < 256 mg/L) Neisseria gonorrhoeae
- Ribosomal methyltransferase-producing Enterobacterales
- Ceftriaxone non-susceptible Salmonella species
- Multidrug-resistant Mycobacterium tuberculosis
- Linezolid non-susceptible Enterococcus species





Conclusions

The establishment of CARAlert in 2016 was a significant enhancement of the AURA Surveillance System, which has provided timely national data on CARs to inform quality improvement initiatives and policies to reduce antimicrobial resistance. As at 31 March 2018, 88 originating laboratories have contributed CARs that have been reported by 24 confirming laboratories. All states and territories have had at least one CAR reported.

CPE reports overall remained steady from October 2017 to March 2018. CPE continue to be dominated by those of the IMP type, found most often in the *E. cloacae* complex. Enterobacterales with multiple types continues to be reported. There was a small outbreak of IMP-producing CPE (*K. pneumoniae* and *E. cloacae*) from six neonates reported in January 2018 from New South Wales. Four KPC were also reported from one institution in Victoria.

The frequency of reporting of CPE highlights the importance of the implementation of the Commission's <u>Recommendations for the control</u> of carbapenemase-producing Enterobacterales: a guide for acute health facilities.⁵

Reports of azithromycin non-susceptible *N. gonorrhoeae* (low-level resistance) showed a steady decline in the six months from 1 October 2017 to 31 March 2018. However, seven *N. gonorrhoeae* with high-level non-susceptibility (MIC > 256 mg/L) were reported; two of which were also ceftriaxone non-susceptible. These reports are concerning because of their implications for a potential outbreak of extremely drug-resistant *N. gonorrhoeae*. The finding highlights the critical importance of sexually transmitted infection prevention and control programs. The data on azithromycin non-susceptible and ceftriaxone non-susceptible N. gonorrhoeae reported to CARAlert complement the comprehensive long term Australian Gonococcal Surveillance Programme which is supported by the Australian Government Department of Health, and state and territory systems that comprise the National Neisseria Network whose role is to monitor and report antimicrobial resistance as part of national surveillance activities to inform treatment guidelines and sexually transmitted infection prevention and control strategies. The increase in notifications of *N. gonorrhoeae* with low-level non-susceptibility peaked in Australia in 2016; a similar increase was also reported internationally in the United States and the United Kingdom.^{6,7,8}

The low background rate of azithromycin nonsusceptible (low-level resistance) *N. gonorrhoeae* in Australia is now well established. Ongoing monitoring of azithromycin and ceftriaxone non-susceptibility is required because of the importance of emerging changes in susceptibility for treatment guidelines.

The increase in multidrug-resistant *Shigella* species that peaked in December 2017 and January 2018, has now subsided.

Other CARs remain at very low levels, providing reassurance that none have become established in Australia.

A review of CARs reported to CARAlert is underway to assess the resistances and species which are currently reported to CARAlert to determine that they continue to be priorities, and identify additional CARs that should be captured by CARAlert.

Enquiries regarding either this report or the CARAlert System should be submitted to CARAlert@safetyandquality.gov.au.

Glossary of terms and abbreviations

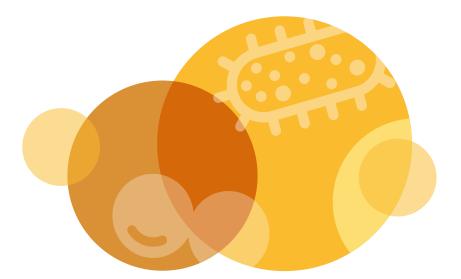
Term/Abbreviation	Definition			
Clinical specimen	Clinical specimens are collected for diagnostic purposes. They include urine, wound, blood and other (e.g. genital or respiratory) specimens			
Screen specimen	Specimens taken for the purpose of screening for resistances			
Confirming laboratory	The laboratory which performs the necessary confirmatory tests for a CAR. Confirming laboratories:			
	 notify the originating laboratory of test outcomes through the usual communication channels, regardless of whether a CAR is confirmed or not. enter data for each confirmed CAR into the CARAlert web-portal. 			
	State and territory health authorities and the Public Health Laboratory Network have contributed to identification of confirming laboratories for the purpose of CARAlert.			
	 notify the originating laboratory of test outcomes through the usual communication channels, regardless of whether a CAR is confirmed or not. 			
	• enter data for each confirmed CAR into the CARAlert web-portal.			
	State and territory health authorities and the Public Health Laboratory Network have contributed to identification of confirming laboratories for the purpose of CARAIert.			
Critical Antimicrobial Resistances (CARs)	CARs are resistance mechanisms, or profiles, known to be a serious threat to the effectiveness of last-line antimicrobial agents			
Originating laboratory	The laboratory to which a specimen is initially referred by a general practice or hospital for routine testing of isolates.			
	If an originating laboratory identifies an isolate that may have the potential to be a CAR, it:			
	 notifies the requesting clinician of the test results, and the suspected CAR 			
	 sends the suspected isolate onto a confirming laboratory for confirmation. 			
AZI (HLR)	azithromycin non-susceptible, high level resistance (HLR, MIC > 256 mg/L) <i>Neisseria gonorrhoeae</i>			
AZI (LLR)	azithromycin non-susceptible, low level resistance (LLR, MIC < 256 mg/L) <i>Neisseria gonorrhoeae</i>			
CPE	carbapenemase-producing Enterobacterales			
CPE+RMT	carbapenemase- and ribosomal methyltransferase-producing Enterobacterales			
CTR NGON	ceftriaxone non-susceptible Neisseria gonorrhoeae			
CTR SALM	ceftriaxone non-susceptible Salmonella species			
DAP SAUR	daptomycin non-susceptible Staphylococcus aureus			
LNZ ENTE	linezolid non-susceptible Enterococcus species			
MDR MTB	multidrug-resistant Mycobacterium tuberculosis			
MDR SHIG	multidrug-resistant Shigella species			
MIC	minimum inhibitory concentration			
RMT	ribosomal methyltransferase-producing Enterobacterales			
VAN SAUR	vancomycin non-susceptible Staphylococcus aureus			



References

- ¹ Lahra MM et al. In press
- ² Whiley DM Lancet. Infectious Diseases. In press
- ³ Australian Commission on Safety and Quality in Health Care. Recommendations for the control of carbapenemase-producing Enterobacterales (CPE). A guide for acute care health facilities. Sydney: ACSQHC, 2017
- ⁴ Australian Commission on Safety and Quality in Health Care (ACSQHC). AURA 2017: Second Australian report on antimicrobial use and resistance in human health. Sydney: ACSQHC; 2017.
- ⁵ Australian Commission on Safety and Quality in Health Care. Recommendations for the control of carbapenemase-producing Enterobacterales (CPE). A guide for acute care health facilities. Sydney: ACSQHC, 2017

- ⁶ Lahra MM. Australian Gonococcal Surveillance Program Quarter 3 2017 Report. Communicable Diseases Intelligence. In press.
- ⁷ Family Planning Association (UK). Sexually Transmitted Infections Factsheet [Internet]; November 2016 [cited 2018 Jun 8]. Available from: <u>https://www.fpa.org.uk/factsheets/</u> sexually-transmitted-infections
- ⁸ Centers for Disease Control (US). 2016 Sexually Transmitted Diseases Surveillance: Gonorrhea [Internet]; [cited 2018 Jun 8]. Available from: <u>https://www.cdc.gov/std/</u> <u>stats16/Gonorrhea.htm</u>



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