AUSTRALIAN COMMISSION ON SAFETY AND QUALITY IN HEALTH CARE

CARAlert Summary Report

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Summary

The Antimicrobial Use and Resistance in Australia (AURA) Surveillance System, coordinated by the Australian Commission on Safety and Quality in Health Care (the Commission), provides essential information to develop and implement strategies to prevent and contain antimicrobial resistance (AMR) in human health and improve antimicrobial use across the acute and community healthcare settings. Funding for AURA is provided by the Australian Government Department of Health and state and territory health departments.

The National Alert System for Critical Antimicrobial Resistances (CARAlert), which was established by the Commission in March 2016, is a key component of the AURA Surveillance System. Participating confirming laboratories submit data to CARAlert on priority organisms with critical resistance to last-line antimicrobial agents. These data support timely response to critical antimicrobial resistances (CARs) by hospitals and state and territory health departments. Some states have stand-alone systems for monitoring selected CARs, which complement CARAlert, but these are not widespread. CARs are resistance mechanisms, or profiles, known not to respond effectively to last-line antimicrobial agents; they are a significant threat to human health.

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

Data Highlights

CPE were the most frequently reported CAR of all CAR types (42.5%), with 2.7% of these also occurring in combination with ribosomal methyltransferases (RMT) (2.7%). CPE reports continue to be dominated by those of the IMP type, found most often in the *Enterobacter cloacae* complex. Azithromycin non-susceptible *Neisseria gonorrhoeae* accounted for 40.5% of CARs during the reporting period.

A total of 691 CARs were reported during this six month period. Compared with the corresponding period in 2017, there was a 9% decrease in the number of CARs reported, a 50% increase in ceftriaxone non-susceptible *Salmonella* species, mostly reported from Victoria (56.7%), and an 86% increase in multidrug-resistant *Shigella* species, mostly reported from NSW (38.5%) and Victoria (30.8%). The proportion of CARs reported from the community and hospital setting (49%) was the same; however, there were differences in the distribution of CAR types between these settings.

One *N. gonorrhoeae* strain with high-level azithromycin non-susceptibility (MIC > 256 mg/L) was confirmed from New South Wales (May 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 three *N. gonorrhoeae* strains reported that were non-susceptible to ceftriaxone, one of which was also azithromycin non-susceptible (low-level resistance, MIC < 256 mg/L), confirmed from Victoria. The detection of these strains is of concern because of the potential public health implications of an outbreak of ceftriaxone non-susceptible *N. gonorrhoeae*.

Implications of key findings and response

The frequency of reporting of CPE highlights the importance of the implementation of the Commission's Recommendations for the control of carbapenemase-producing Enterobacterales: a guide for acute health facilities.[2]

Effective surveillance of *N. gonorrhoeae* AMR, continuation of sexually transmitted infection prevention and control programs, and outbreak response strategies are all key to minimising the spread of infections that are difficult to treat.

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.

Each state and territory health department has designated officers who have access to the CARAlert database to enable detailed review of CARs reported for their jurisdiction, including the name of the public hospital where a patient with a confirmed CAR was cared for. This information assists states and territories to determine whether infection prevention and control and/or follow-up response action is required.

The Commission is working with the Department of Health and all states and territories on establishment of a coordinated network for the response to outbreaks of resistant organisms in Australia. CARAlert will be one of the data sources to inform this process.

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Introduction

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. These CARs were drawn from the list of high-priority organisms and antimicrobials which are the focus of the AURA Surveillance System.[3]

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 April 2018 and 30 September 2018 and the results reported into CARAlert by 31 October 2018. It complements the CARAlert updates and reports 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.

For this report, the state or territory is determined, in the first instance, as the state or territory within which the hospital where the CAR was reported is located. Where this information has not been entered, or if the source of the isolate is from the community, the patient's state or territory of residence is used.

Critical antimicrobial resistances reported by state and territory

Between 1 April 2018 and 30 September 2018, 691 results from 64 originating laboratories across Australia were entered in the CARAlert system (Table 2).

Carbapenemase-producing Enterobacterales (CPE) were the most frequently reported CAR of all CAR types (42.5%) with 2.7% of these also occurring in combination with ribosomal methyltransferases (RMT). Azithromycin non-susceptible *Neisseria gonorrhoeae* accounted for 40.5% of CARs during the reporting period**.** There were no reports of linezolid non-susceptible or vancomycin non-susceptible *Staphylococcus aureus* during this reporting period.

The majority of CARs continue to be reported from Victoria (37.4%), New South Wales (31.4%), and Queensland (19.1%). CARs were the lowest in South Australia (9), Tasmania (3), and the Northern Territory (3); only 2.2% (15/691) of all CARs were reported from these states and territories. Seven reports were from overseas residents; three CPE, one CPE+RMT, one azithromycin non-susceptible (low-level resistance [LLR] <256 mg/L) *N. gonorrhoeae*, one linezolid non-susceptible *Enterococcus* species, and one multidrug-resistant *Mycobacterium tuberculosis*.

Although the total number of CARs reported was 9% lower than for the corresponding reporting period last year, there was an increase of 50% in ceftriaxone non-susceptible *Salmonella* species the majority reported from Victoria (56.7%), and an 86% increase in multidrug-resistant *Shigella* species, mostly reported from NSW (38.5%) and Victoria (30.5%).

Table 2: Number of critical antimicrobial resistance isolates, by state and territory, 1 April 2018 to 30 September 2018

Critical antimicrobial resistance	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	OS	1 April – 30 September			1 January – 30 September		
										2018	2017	Relative change*	2018	2017	Relative change*
Azithromycin non-susceptible (LLR < 256 mg/L) *Neisseria gonorrhoeae*	110	129	32	1	7	0	0	0	1	280	342	-18.1%	391	591	-33.8%
Carbapenemase-producing Enterobacterales	79	67	84	6	28	1	2	8	0	275	307	-10.4%	411	418	-1.7%
Daptomycin non-susceptible *Staphylococcus aureus*	9	24	5	0	14	0	0	0	0	52	45	+15.6%	85	81	+4.9%
Ceftriaxone non-susceptible *Salmonella* species	5	17	6	0	0	1	0	1	0	30	20	+50.0%	43	24	79.2%
Carbapenemase and ribosomal methyltransferase-producing Enterobacterales	3	12	1	2	0	1	0	0	0	19	18	+5.6%	21	21	0.0%
Multidrug-resistant *Shigella* species	5	4	1	0	2	0	0	1	0	13	7	+85.7%	36	12	200.0%
Linezolid non-susceptible *Enterococcus* species	4	2	0	0	0	1	0	1	0	8	2	+300.0%	12	3	300.0%
Ribosomal methyltransferase-producing Enterobacterales	0	5	1	0	0	0	0	0	0	6	11	-45.5%	7	16	-56.3%
Multidrug-resistant *Mycobacterium tuberculosis*	0	1	2	1	0	0	0	0	0	4	4	0.0%	6	8	-25.0
Ceftriaxone non-susceptible *Neisseria gonorrhoeae*	0	2	0	0	0	0	0	0	0	2	0	–	2	0	–
Ceftriaxone non-susceptible and azithromycin non-susceptible (LLR < 256 mg/L) *Neisseria gonorrhoeae*	0	1	0	0	0	0	0	0	0	1	0	–	1	0	–
Azithromycin non-susceptible (HLR > 256 mg/L) *Neisseria gonorrhoeae*	1	0	0	0	0	0	0	0	0	1	4	-75.0%	6	4	50.0%
Ceftriaxone non-susceptible and azithromycin non-susceptible (HLR > 256 mg/L) *Neisseria gonorrhoeae*	0	0	0	0	0	0	0	0	0	0	0	–	2	0	–
Linezolid non-susceptible *Staphylococcus aureus*	0	0	0	0	0	0	0	0	0	0	0	–	1	0	–
Total (as at 31 October 2018)	**216**	**264**	**132**	**10**	**51**	**4**	**2**	**11**	**1**	**691**	**760**	**-9.1%**	**1,024**	**1,178**	

HLR = high-level resistance; LLR = low-level resistance; OS = overseas;; – = not applicable

* Relative change = absolute change between period in 2017 and same period in 2018, expressed as a percentage of 2017 base

Critical antimicrobial resistances by species and month

The number and distribution of CARs reported nationally, and by state and territory, from 1 April 2018 to 30 September 2018, is shown in Figure 1. There was an average of 115 entries per month (range 93–126), with notable state and territory variation.

Figure 1. Critical antimicrobial resistances, number and distribution reported nationally, by state and territory, and by month, 1 April 2018 to 30 September 2018

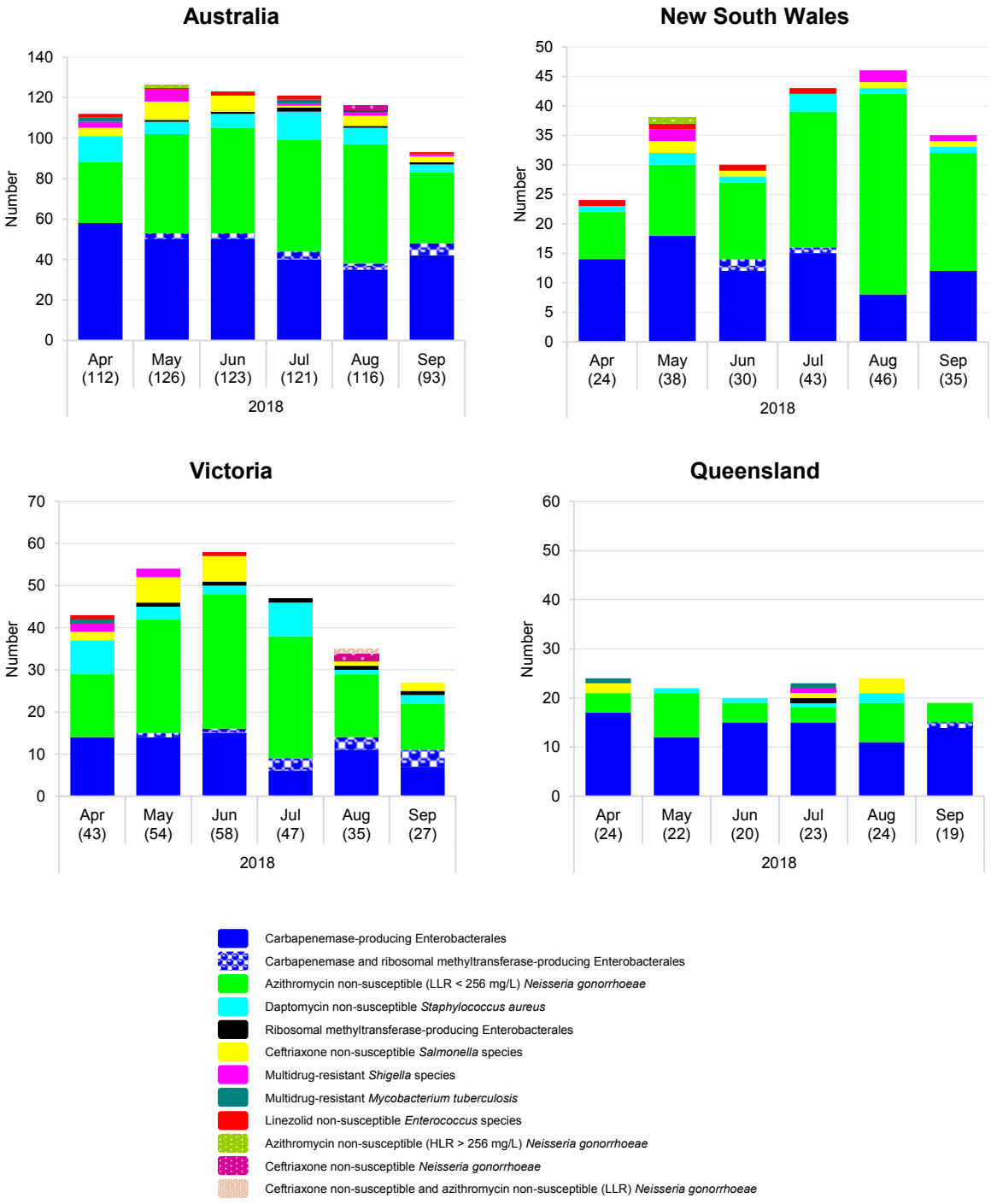
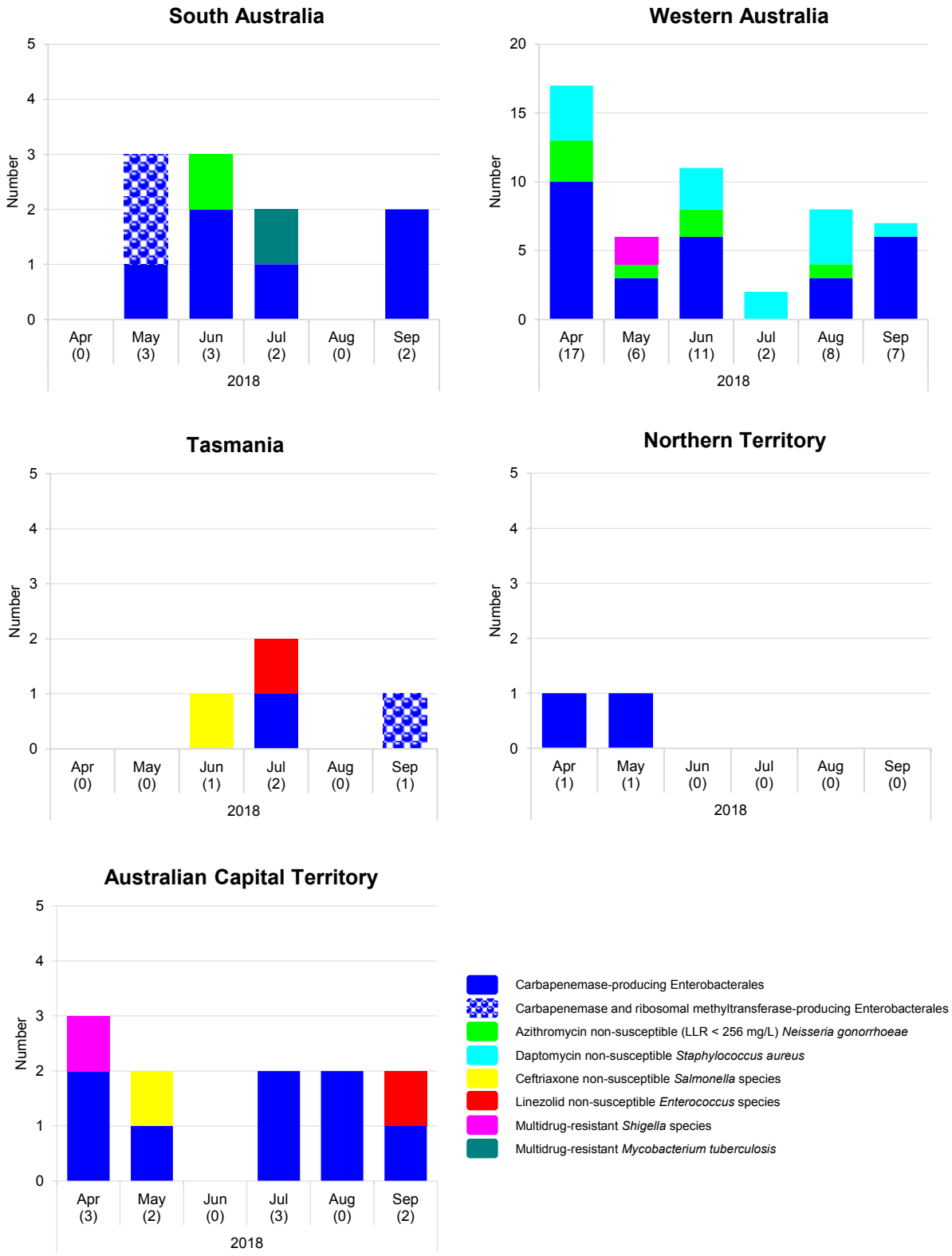


Figure 1. (continued). Critical antimicrobial resistances, number and distribution reported nationally, by state and territory, and by month, 1 April 2018 to 30 September 2018



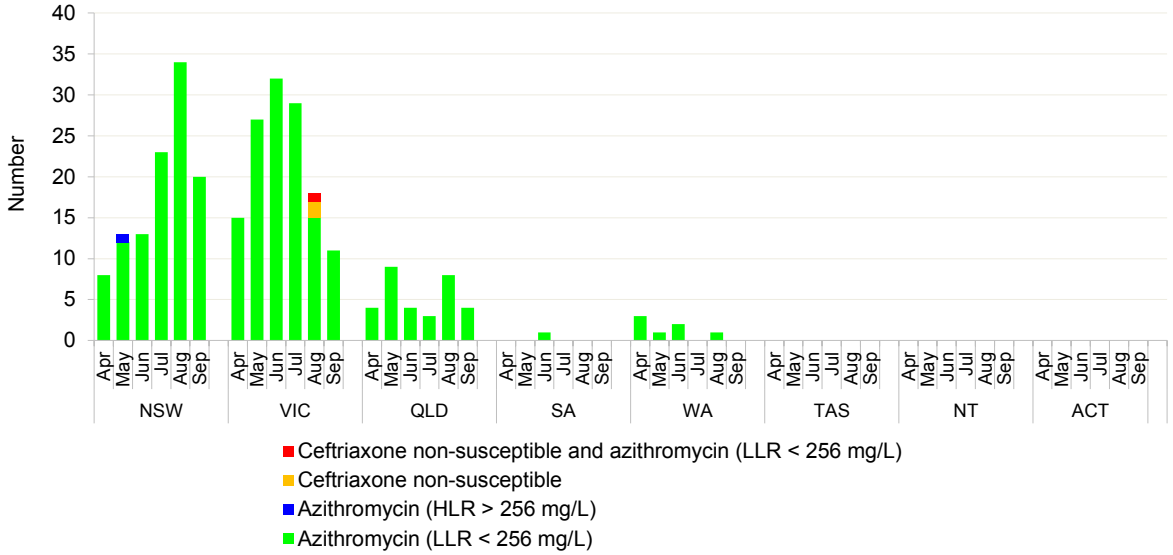
Nationally, CPE were the most frequent CAR reported for April, May and September 2018; during July and August 2018, azithromycin non-susceptible *N. gonorrhoeae* dominated.

Reports of multidrug-resistant *Shigella* species have now declined to levels seen before peak that was observed during December 2017–February 2018.

Daptomycin non-susceptible *S. aureus* were reported from four states/territories, with 46% (24/52) from Victoria, and 27% (14/52) from Western Australia.

Reports of azithromycin non-susceptible *N. gonorrhoeae* originating from New South Wales peaked during August 2018 (Figure 2). One strain with high-level azithromycin non-susceptibility (MIC > 256 mg/L) was confirmed from New South Wales (May 2018). Three *N. gonorrhoeae* that were ceftriaxone non-susceptible were reported from three patients; one strain was also azithromycin non-susceptible (low-level resistance, MIC < 256 mg/L). All three patients resided in Victoria.

Figure 2. *Neisseria gonorrhoeae*, number reported by state and territory, and month of collection*, 1 April 2018 to 30 September 2018

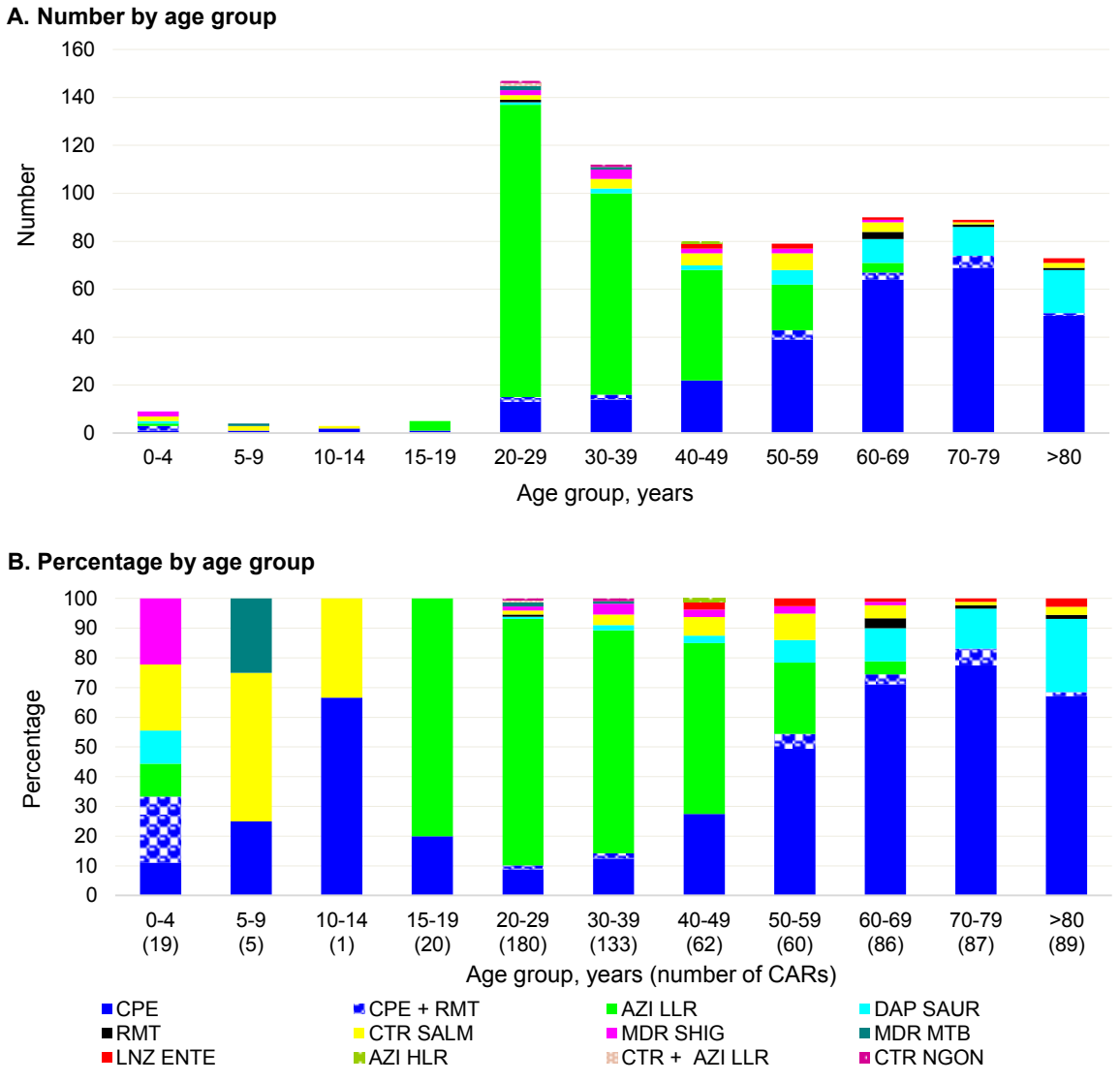


* Where state and territory of residence is unknown, the state of the originating laboratory has been assigned

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 group of 40–49 years (Figure 3). Sixty-five per cent (191/294) of CPE were from people aged 60 years and older. Azithromycin non-susceptible *N. gonorrhoeae* were the predominant CAR reported for the age groups 15–19 years, 20–29 years, 30–39 years and 40–49 years. Two per cent (16/691) of all CARs were reported in children aged less than 15 years. Among this age group, CPE (31.3%), ceftriaxone non-susceptible *Salmonella* species (12.5%), and multidrug-resistant *Shigella* species were the most common in this age group. The distribution of CARs across the age groups has remained consistent since the commencement of the program.

Figure 3. Critical antimicrobial resistances, number (A) and percentage (B) by age group, 1 April 2018 to 30 September 2018



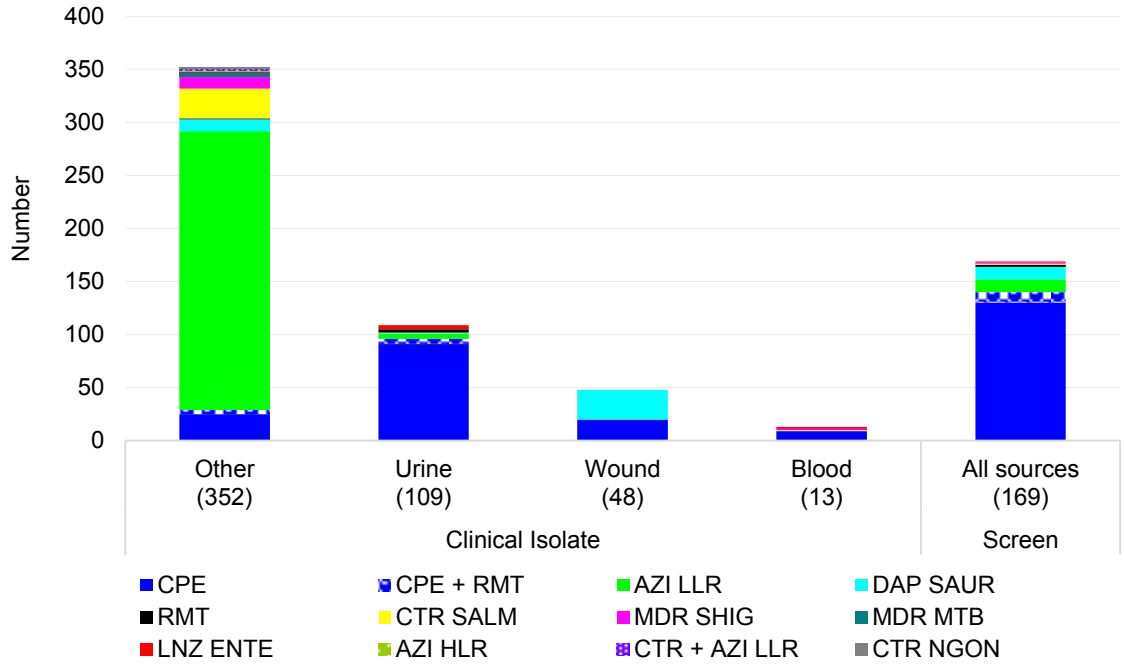
AZI LLR = azithromycin non-susceptible, low-level resistance (LLR, MIC < 256 mg/L) *Neisseria gonorrhoeae*; AZI HLR = azithromycin non-susceptible, high-level resistance (HLR, MIC > 256 mg/L) *Neisseria gonorrhoeae*; CPE = carbapenemase-producing Enterobacterales; CPE+RMT = carbapenemase- and ribosomal methyltransferase-producing Enterobacterales; CTR + AZI LLR = ceftriaxone non-susceptible and azithromycin non-susceptible, low-level resistance (LLR, MIC < 256 mg/L); 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

Over 75% 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-two per cent (154/294) of CPE isolates were from clinical specimens; 62% (96/154) of these were from urine, and 6% (9/154) from blood cultures. CPE is the most common CAR reported in blood stream isolates. The only other CARs reported from blood cultures were one ceftriaxone non-susceptible *Salmonella* Typhi, one multidrug-resistant *Shigella flexneri*, one linezolid non-susceptible *Enterococcus faecium*, and one linezolid non-susceptible *Enterococcus faecalis*.

Figure 4. Critical antimicrobial resistances, number reported by specimen type, 1 April 2018 to 30 September 2018



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

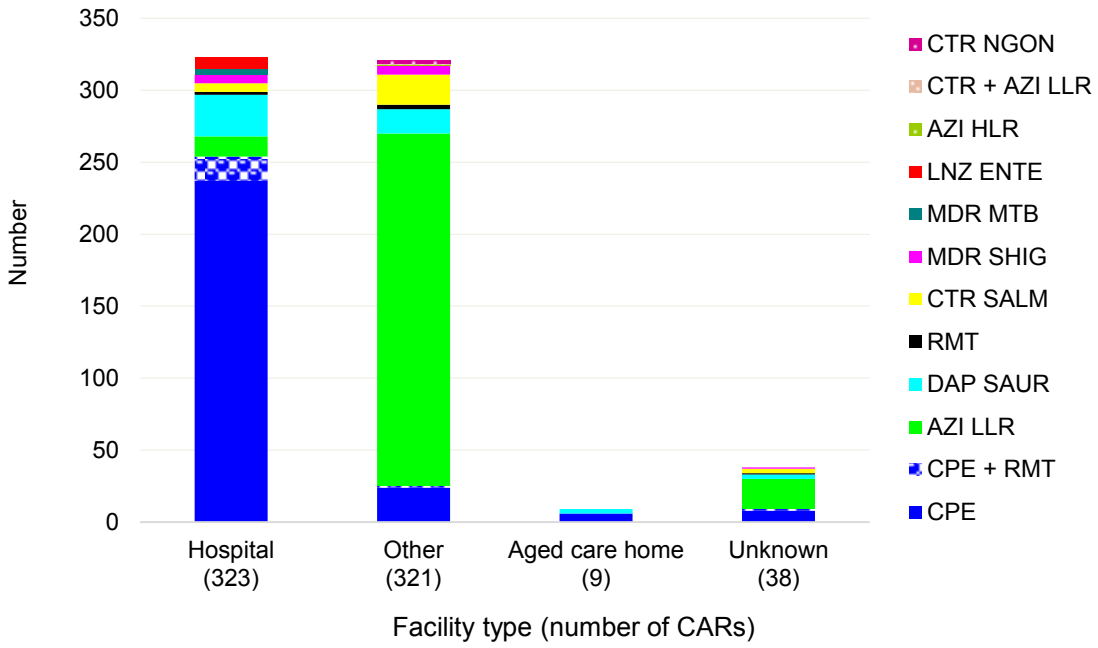
AZI LLR = azithromycin non-susceptible, low-level resistance (LLR, MIC < 256 mg/L) *Neisseria gonorrhoeae*; AZI HLR = azithromycin non-susceptible, high-level resistance (HLR, MIC > 256 mg/L) *Neisseria gonorrhoeae*; CPE = carbapenemase-producing Enterobacterales; CPE+RMT = carbapenemase- and ribosomal methyltransferase-producing Enterobacterales; CTR + AZI LLR = ceftriaxone non-susceptible and azithromycin non-susceptible, low-level resistance (LLR, MIC < 256 mg/L); 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

Where setting was known, the proportion of CARs detected in hospitalised patients or hospital outpatients (49%, 323/653) was the same as those detected in the community setting (49%, 321/653). One per cent of reported CARs (9/653) were from aged care home residents (Figure 5).

Seventy-nine percent (254/323) of the CARs detected in hospitalised patients were CPE; of the nine CARs in aged care home residents, only CPE (6) and daptomycin non-susceptible *S. aureus* (3) were reported. Azithromycin non-susceptible *N. gonorrhoeae* was the most common CAR reported for isolates collected in community settings. Facility type for the community setting is 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 type of facility the patient attended for treatment.

Figure 5. Critical antimicrobial resistances, number reported by facility type, 1 April 2018 to 30 September 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 LLR = ceftriaxone non-susceptible and azithromycin non-susceptible, low-level resistance (LLR, MIC < 256 mg/L); 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

Carbapenemase-producing Enterobacterales were reported from all states and territories. Seven different carbapenemase types (IMP, NDM, OXA-48-like, KPC, OXA-23-like, VIM, and GES) were reported throughout Australia. Three carbapenemase types – IMP (55%, 161/294), NDM (22%, 65/294), and OXA-48-like (13%, 39/2294) alone – accounted for 90% of all Enterobacterales with a confirmed carbapenemase. Nine Enterobacterales had multiple types (NDM+OXA-48-like [7]; IMP+NDM [1]; KPC+OXA-48-like [1]. Thirteen of 16 KPC reported were from Victoria; nine were from one institution, and six of these were collected in April 2018.

Regional differences in the carbapenemase types reported are shown in Figure 6. The distribution of carbapenemase types by state and territory and month of collection is shown in Figure 7. The twelve-month trend data for the top four carbapenemase types is shown Figure 8.

IMP type carbapenemases comprised the majority of CPE in Queensland (78%, 66/88), New South Wales (67%, 55/82), Western Australia (54%, 15/28), and the Australian Capital Territory (88%, 7/8). All the isolates that were genetically sequenced (50%, 81/161) were $bla_{\text{IMP-4}}$. IMP-producing Enterobacterales were reported from 50 hospitals across Australia; nine of which had more than five isolates reported during the six-month reporting period.

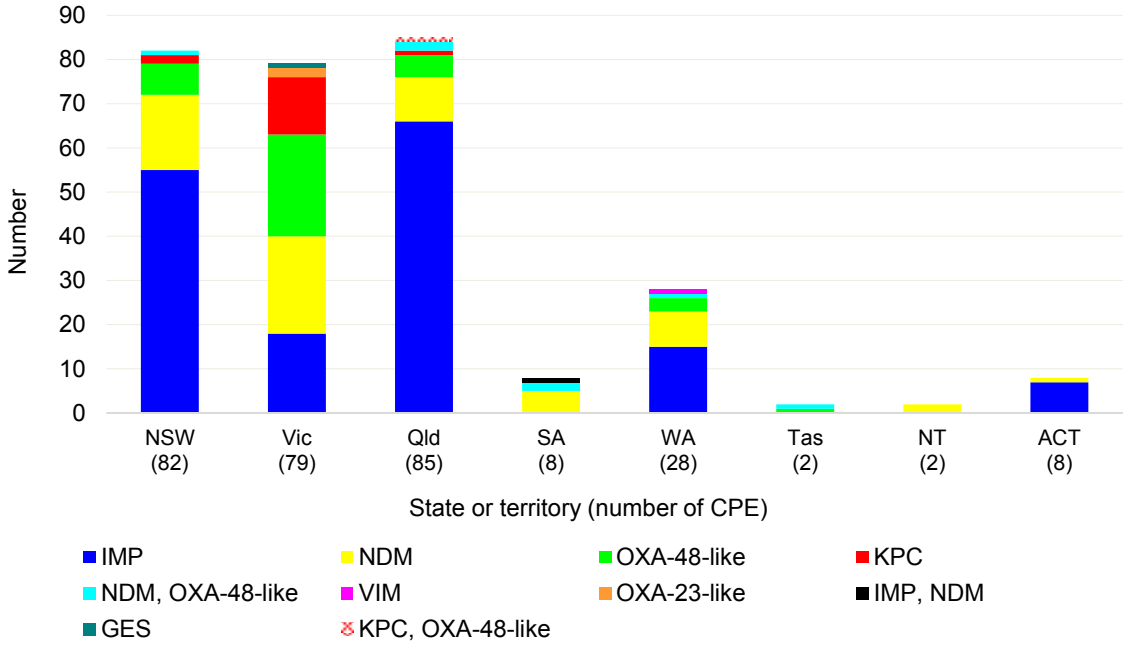
NDM types are of particular importance because of their resistance phenotype compared to other CPEs. NDM types were reported from all states and territories, and comprised 25% (73/294) of all CPE in this reporting period. All eight CPE reported from South Australia were NDM types, however no epidemiological links were found. NDM were not reported from South Australia in the preceding reporting period (1 October 2017 to 31 March 2018). NDM+OXA-48-like Enterobacterales [7] were reported from five states (Table 3). Three different NDM genes were found in the isolates sequenced in this reporting period: $bla_{\text{NDM-5}}$ (60%, 18/30), $bla_{\text{NDM-1}}$ (33%, 10/30), and $bla_{\text{NDM-7}}$ (7%, 2/30).

OXA-48-like CPE reports are becoming more frequent (Figure 8). There was a spike in reports in the second and third quarters of 2017 due to a local outbreak of OXA-48 producing *E. coli* ST38 in Queensland, otherwise reports have steadily increased to more than double, compared to the same period in 2016 (47 versus 24 reports).

Co-production of CPE types is seen at low levels (3%, 41/1,326); South Australia has reported two instances of NDM+OXA-48-like combination, the first since late October 2016, whilst Tasmania and Queensland have reported this for the first time in this reporting period. The most common co-producing genes since March 2016 are NDM+OXA-48-like (75.6%, 31/41), NDM+KPC (3), OXA-48-like+IMP (3), IMP+KPC (1), IMP+NDM (1), KPC+OXA-48-like (1) and NDM+VIM (1).

Ribosomal methyltransferases were often detected among isolates containing NDM types (19%, 14/73; *rmtB* [9], *armA* [2], *rmtC* [1], *rmtF* [1] and *armA*+*rmtB* [1]).

Figure 6. Carbapenemase-producing Enterobacterales*, by carbapenemase type, number reported by state and territory, 1 April 2018 to 30 September 2018



* Carbapenemase-producing Enterobacterales (n = 275), carbapenemase- and ribosomal methyltransferase-producing Enterobacterales (n = 19)

Figure 7. Carbapenemase types, number reported by month and state and territory, 1 April 2018 to 30 September 2018

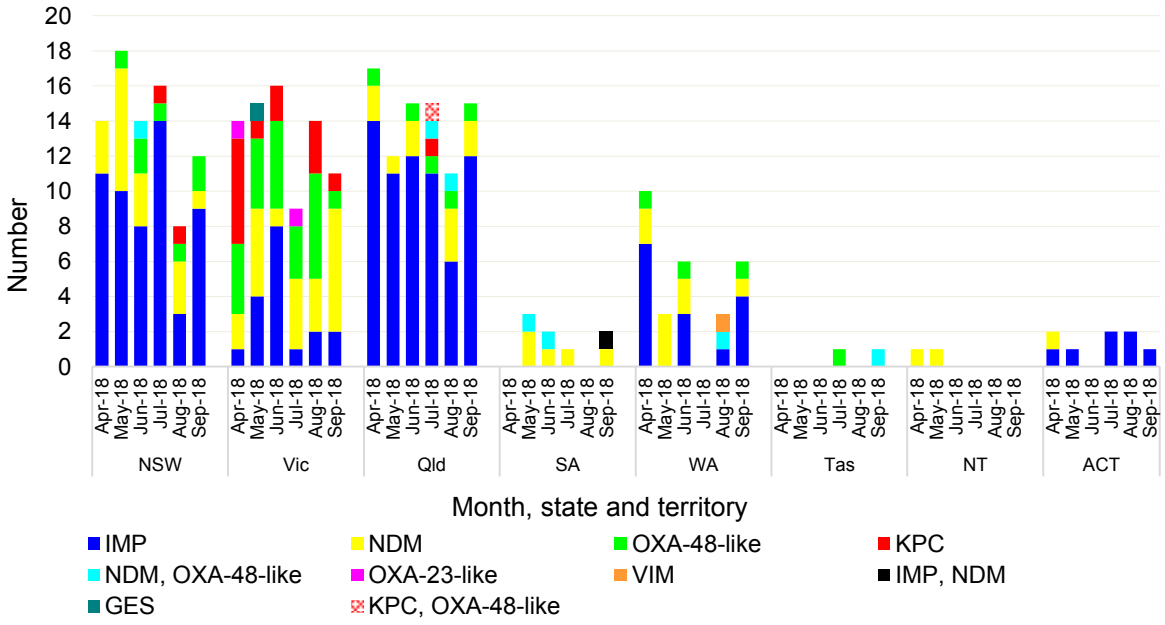


Table 3: Number of carbapenemase types, by state and territory, 1 April 2018 to 30 September 2018

Carbapenemase type	NSW	VIC	QLD	SA	WA	TAS	NT	ACT	Total
IMP	55	18	66	0	15	0	0	7	161
NDM	17	22	10	5	8	0	2	1	65
NDM	15	14	9	4	8	0	2	1	53
NDM, rmtB	0	7	1	0	0	0	0	0	8
NDM, armA	2	0	0	0	0	0	0	0	2
NDM, rmtF	0	0	0	1	0	0	0	0	1
NDM, rmtC	0	1	0	0	0	0	0	0	1
OXA-48-like	7	23	5	0	3	1	0	0	39
OXA-48-like	6	19	5	0	3	1	0	0	34
OXA-48-like, armA	0	4	0	0	0	0	0	0	4
OXA-48-like, rmtB	1	0	0	0	0	0	0	0	1
KPC	2	13	1	0	0	0	0	0	16
NDM, OXA-48-like	1	0	2	2	1	1	0	0	7
NDM, OXA-48-like	1	0	2	1	1	0	0	0	5
NDM, OXA-48-like, rmtB	0	0	0	1	0	0	0	0	1
NDM, OXA-48-like, armA, rmtB	0	0	0	0	0	1	0	0	1
OXA-23-like	0	2	0	0	0	0	0	0	2
VIM	0	0	0	0	1	0	0	0	1
IMP, NDM	0	0	0	1	0	0	0	0	1
GES	0	1	0	0	0	0	0	0	1
KPC, OXA-48-like	0	0	1	0	0	0	0	0	1
Total CPE	**82**	**79**	**85**	**8**	**28**	**2**	**2**	**8**	**294**

Figure 8. Two–year trend data for the top four carbapenemase types, by state and territory and nationally, 1 October 2016 to 30 September 2018

Type	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
IMP	11 5	8 2	12 7	0 0	4 0	0 0	0 0	3 0	30 20
NDM	4 0	5 1	2 0	1 0	2 0	0 0	1 0	1 0	13 4
OXA-48-like	2 0	5 1	26 0	0 0	1 0	0 0	0 0	0 0	29 2
KPC	1 0	3 0	0 0	0 0	0 0	0 0	0 0	0 0	4 1
All types	16 7	18 8	38 8	2 0	6 1	1 0	1 0	3 1	75 31

Line graphs represent three-month moving average for the period 1 October 2016 to 30 September 2018, for each type, where maximum monthly average was greater than one. Straight line indicates no isolates reported. Where maximum monthly average was less than one, lines are not represented

Carbapenemase-producing Enterobacterales by species and carbapenemase type

Carbapenemases were found in 16 species of Enterobacterales representing eight genera (*Citrobacter*, *Enterobacter*, *Escherichia*, *Klebsiella*, Proteus, *Providencia*, *Raoultella*, and *Serratia*). *E. coli* (28%, 83/294), *K. pneumoniae* (27%, 79/294), and *E. cloacae* complex (26%, 76/294), and contributed to 81% all species (Figure 9).

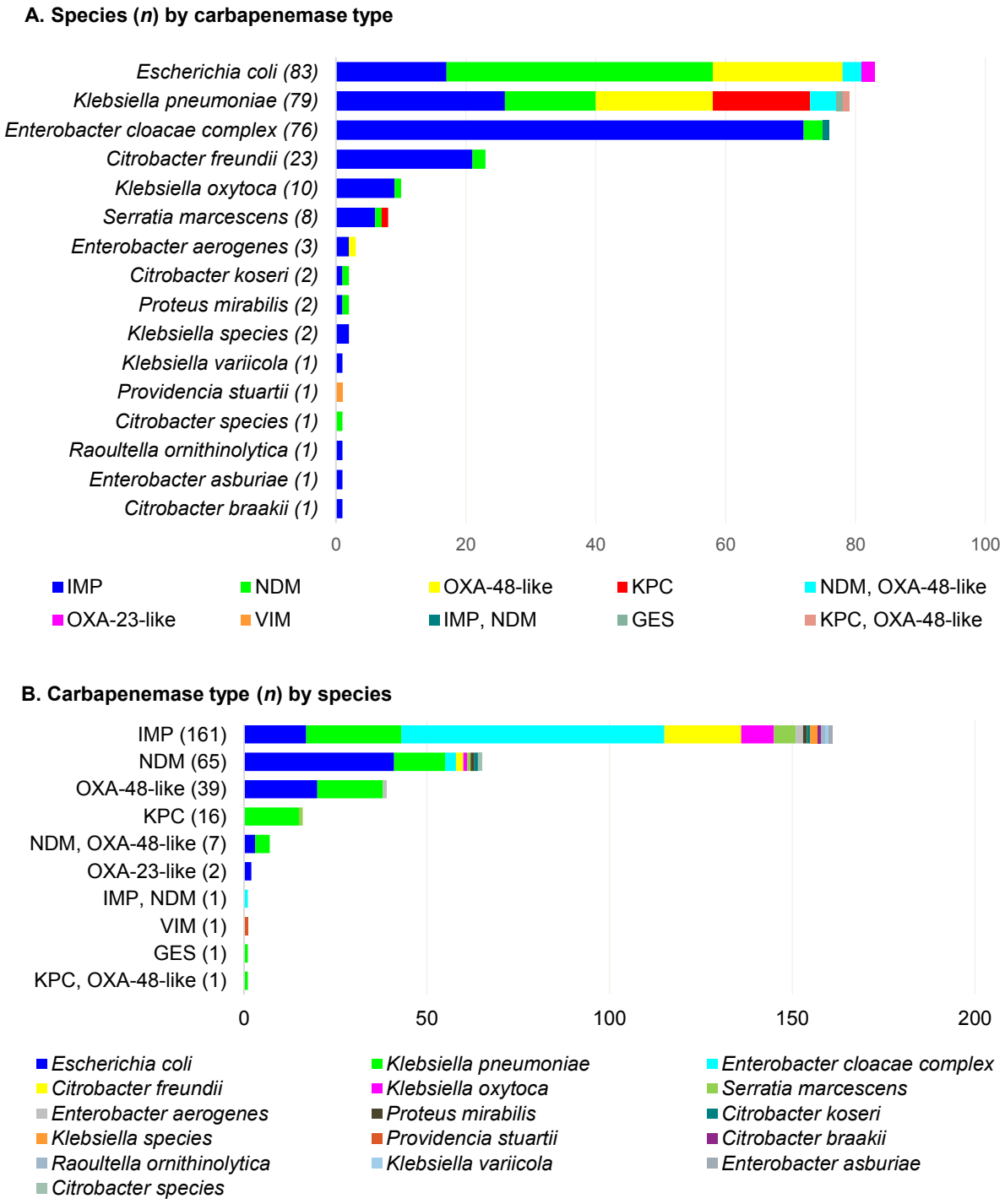
IMP-types were found in 14 different species and accounted for 54.8% (161/294) of all carbapenemases. *E. cloacae* complex accounted for 45% (72/161) of all IMP types. NDM-types were found in 22.1% (65/294) of all CPE, mainly in *E. coli* (63%, 41/65). OXA-48-like types, when detected alone, were found in mainly in *E. coli* (51%, 20/39) and *K. pneumoniae* (46%, 18/39).

Fifteen of 16 KPC were found in *K. pneumoniae*; 13 of these were reported from Victoria. One *K. pneumoniae* isolate harbouring both KPC and OXA-48 was detected from a patient residing in Queensland.

Two *E. cloacae* complex harbouring OXA-23-like was detected from two patients residing in Victoria.

One GES-5 producing *K. pneumoniae* was reported in May 2018 from a patient hospitalised in Victoria.

Figure 9. Carbapenemase-producing Enterobacterales*, number reported by (A) species and (B) carbapenemase type, 1 April 2018 to 30 September 2018



* Carbapenemase-producing Enterobacterales (n = 275), carbapenemase- and ribosomal methyltransferase-producing Enterobacterales (n = 19)

Other Critical Antimicrobial Resistance types

RMT were detected in 25 Enterobacterales, across five different species; 76% (19/25) of these isolates also harboured a carbapenemase. Four RMT genes were found: *rmtB* (52%; 13/25); *armA* (28%; 7/25), *rmtC* (12%, 3/25), and *rmtF* (4%; 1/25); one isolate contained both *armA*+*rmtB*. Sixty-eight per cent (17/25) of all RMT were reported from Victoria; with 71% (12/17) in combination with NDM [8] or OXA-232 (OXA-48-like) [4] carbapenemase types.

Thirty ceftriaxone non-susceptible *Salmonella* species were confirmed from Victoria (17), Queensland (6), New South Wales (5), Tasmania (1) and the Australian Capital Territory (1). Eighteen had an ESBL either alone (17) or with a plasmid-borne *ampC* gene (1); 12 had plasmid-borne *ampC* alone. Six (20%, 6/30) were isolated from hospitalised patients. One *Salmonella* Typhi with CTX-M-15 was reported from a hospitalised patient (age group 10-14 years) residing in Tasmania, who had a history of overseas travel. All other species were non-typhoidal.

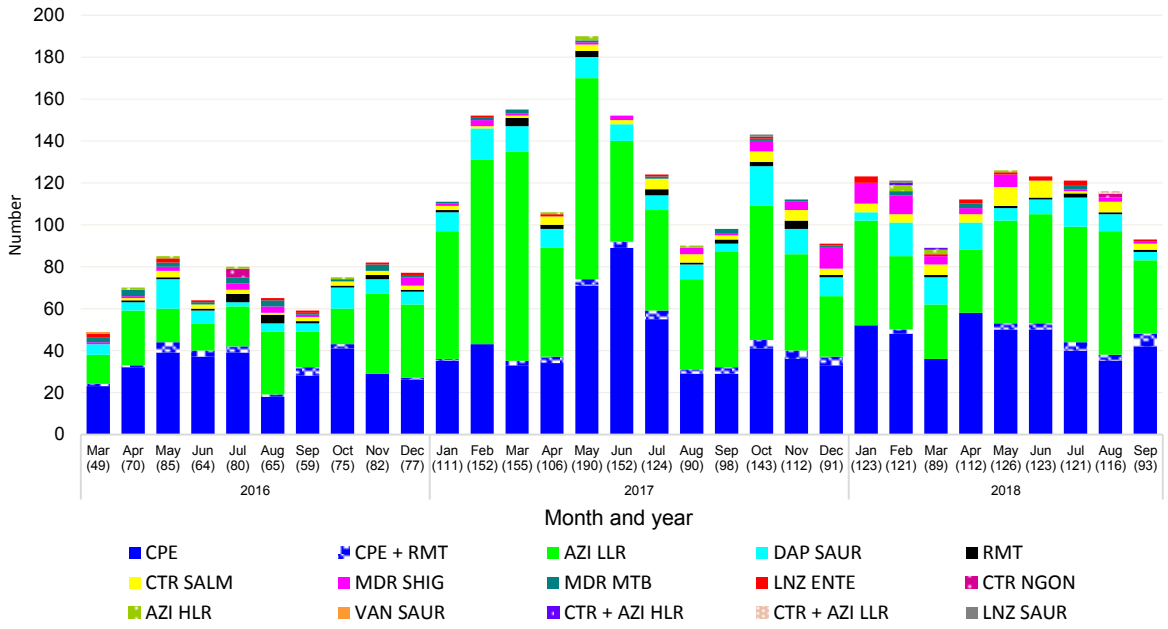
There were 13 reports of multidrug resistant *Shigella* species (*S. sonnei* [9], *S. flexneri* [4]) from patients residing in New South Wales (5), Victoria (4), Western Australia (2), Queensland (1), and the Australian Capital Territory (1).

Eight linezolid non-susceptible *Enterococcus* species were reported; five were *E. faecalis*, and three were *E. faecium*. All reports from New South Wales were *E. faecalis* (4).

Trends since March 2016

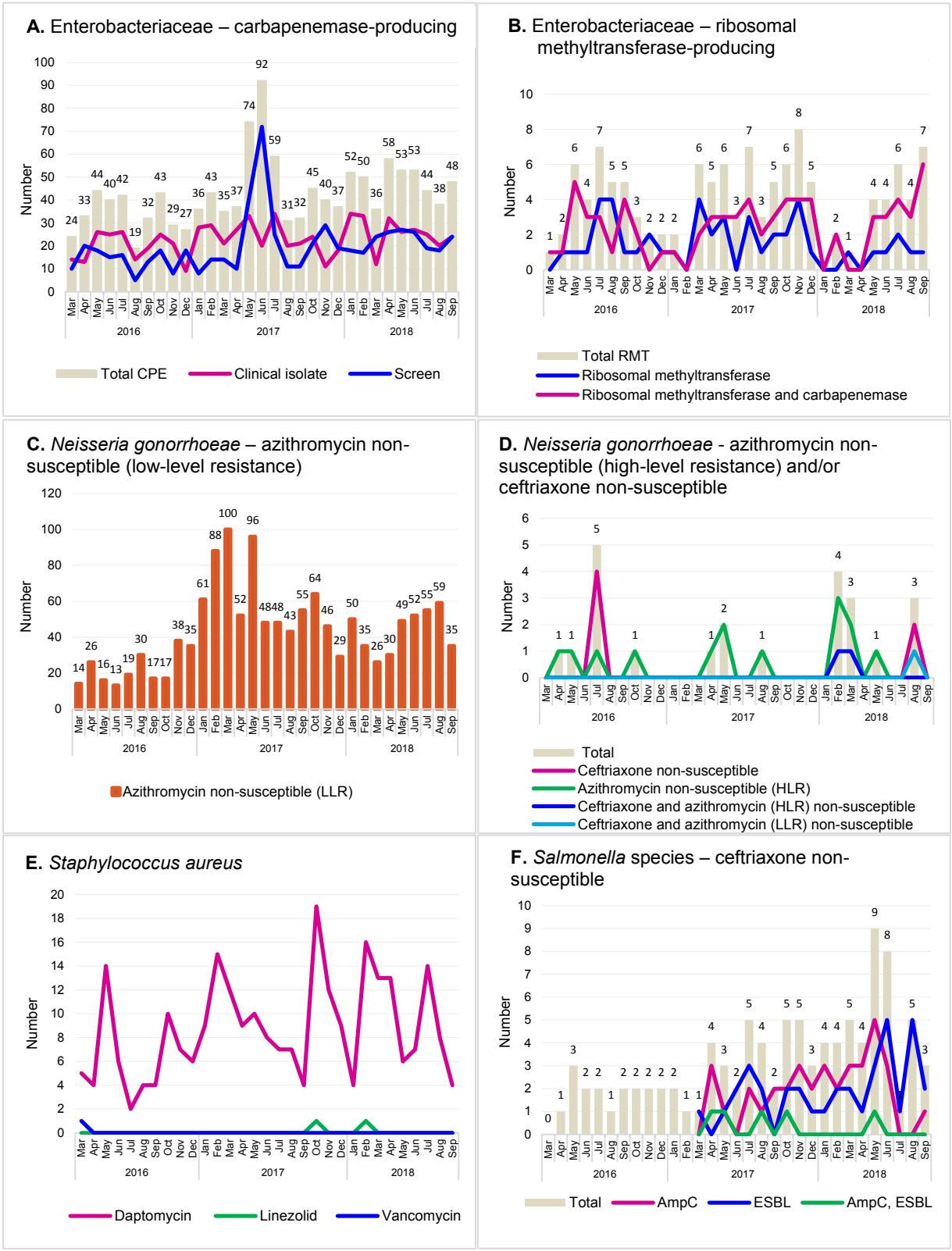
The proportion of CARs associated with priority organisms since 17 March 2016 is shown in Figure 10. The number of CARs reported by species and month is shown in Figure 11. The number and proportion reported nationally, and by state and territory is shown in Figure 12. The fluctuations in reporting of CARs, particularly CPE and azithromycin non-susceptible *N. gonorrhoeae*, and state and territory variations have already been noted.

Figure 10. Critical antimicrobial resistances (CARs), as a percentage of all CARs, reported by month, 17 March 2016–30 September 2018



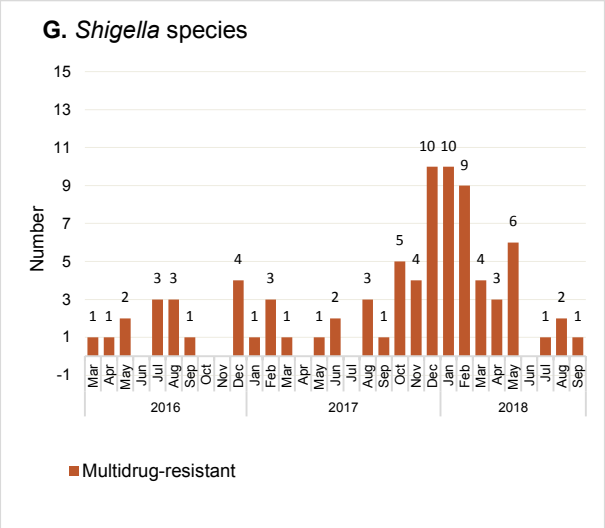
AZI LLR = azithromycin non-susceptible, low-level resistance (LLR, MIC < 256 mg/L) *Neisseria gonorrhoeae*; AZI HLR = azithromycin non-susceptible, high-level resistance (HLR, MIC > 256 mg/L) *Neisseria gonorrhoeae*; CPE = carbapenemase-producing Enterobacterales; CPE + RMT = carbapenemase- and ribosomal methyltransferase-producing Enterobacterales; CTR + AZI LLR = ceftriaxone non-susceptible and azithromycin non-susceptible, low-level resistance (LLR, MIC < 256 mg/L); CTR + AZI HLR = ceftriaxone non-susceptible and azithromycin non-susceptible, high-level resistance (HLR, MIC > 256 mg/L); 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 non-susceptible *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

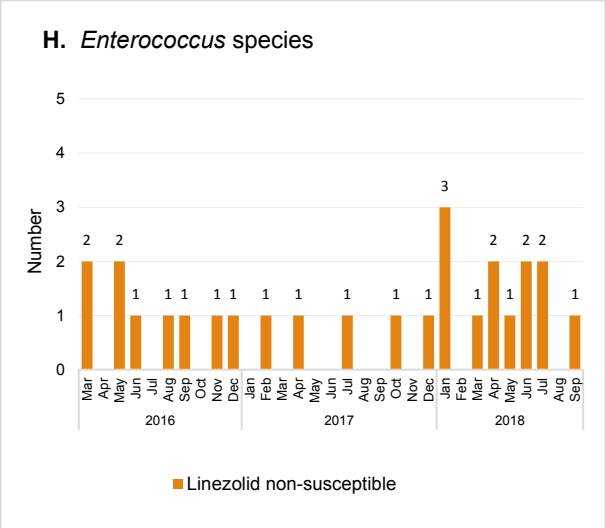
Figure 11. Critical antimicrobial resistances, number reported by species and month, 17 March 2016–30 September 2018



CPE = carbapenemase-producing-Enterobacterales; ESBL = extended-spectrum β-lactamase; RMT = ribosomal methyltransferase-producing Enterobacterales; LLR = low-level resistance; HLR = high-level resistance

Figure 11 (continued). Critical antimicrobial resistances, number reported by species and month, 17 March 2016–30 September 2018





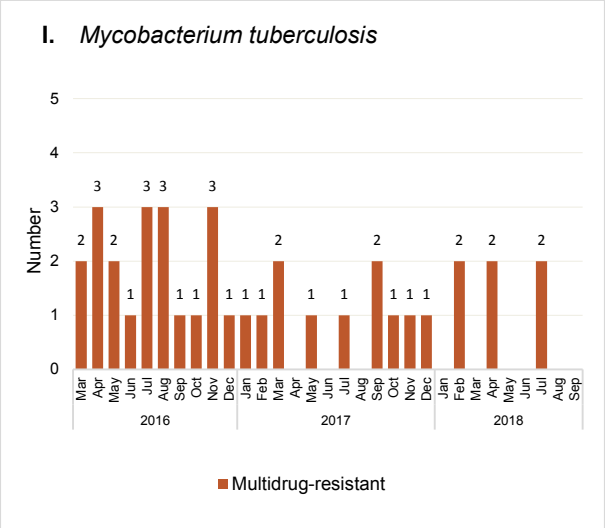
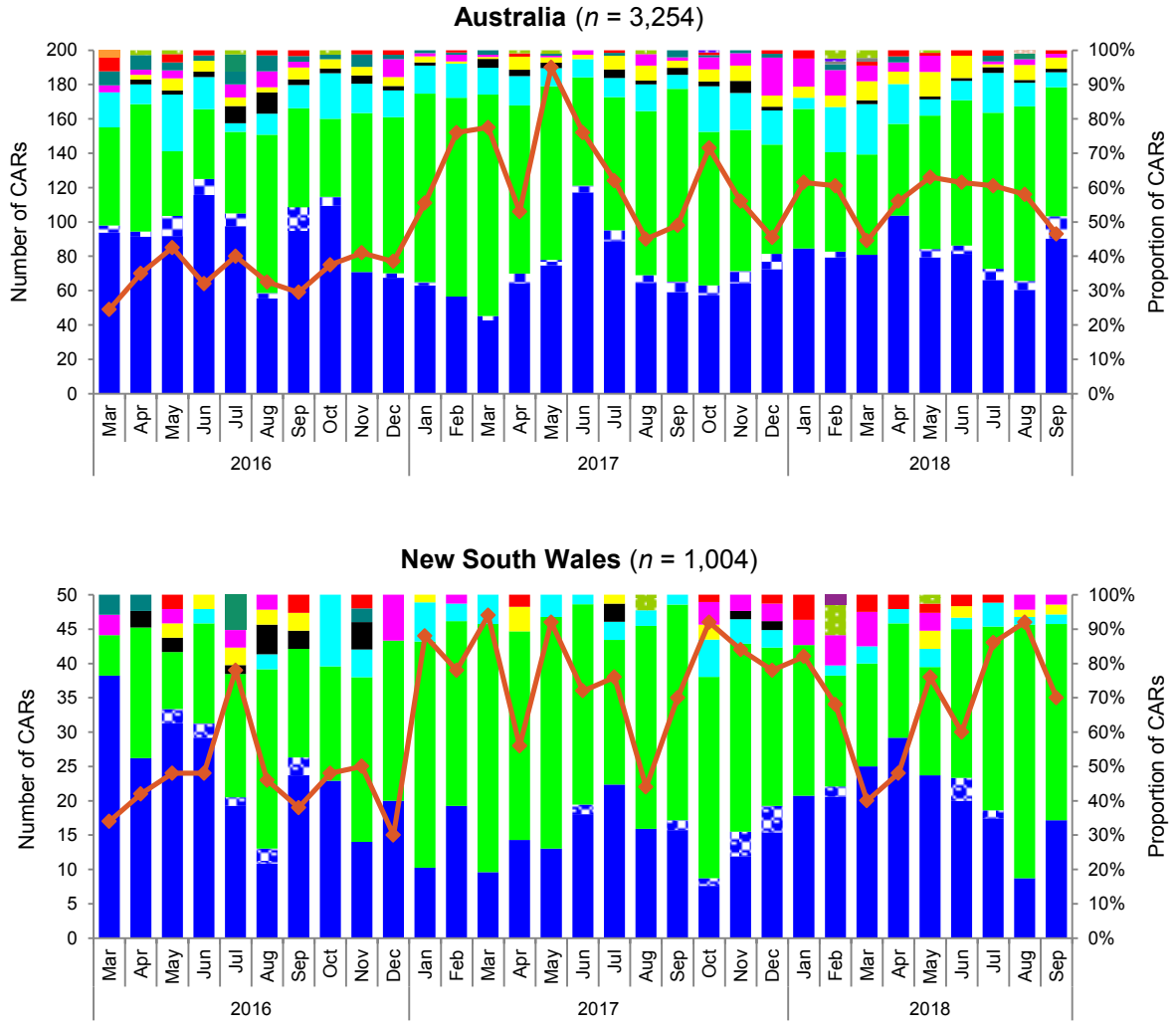


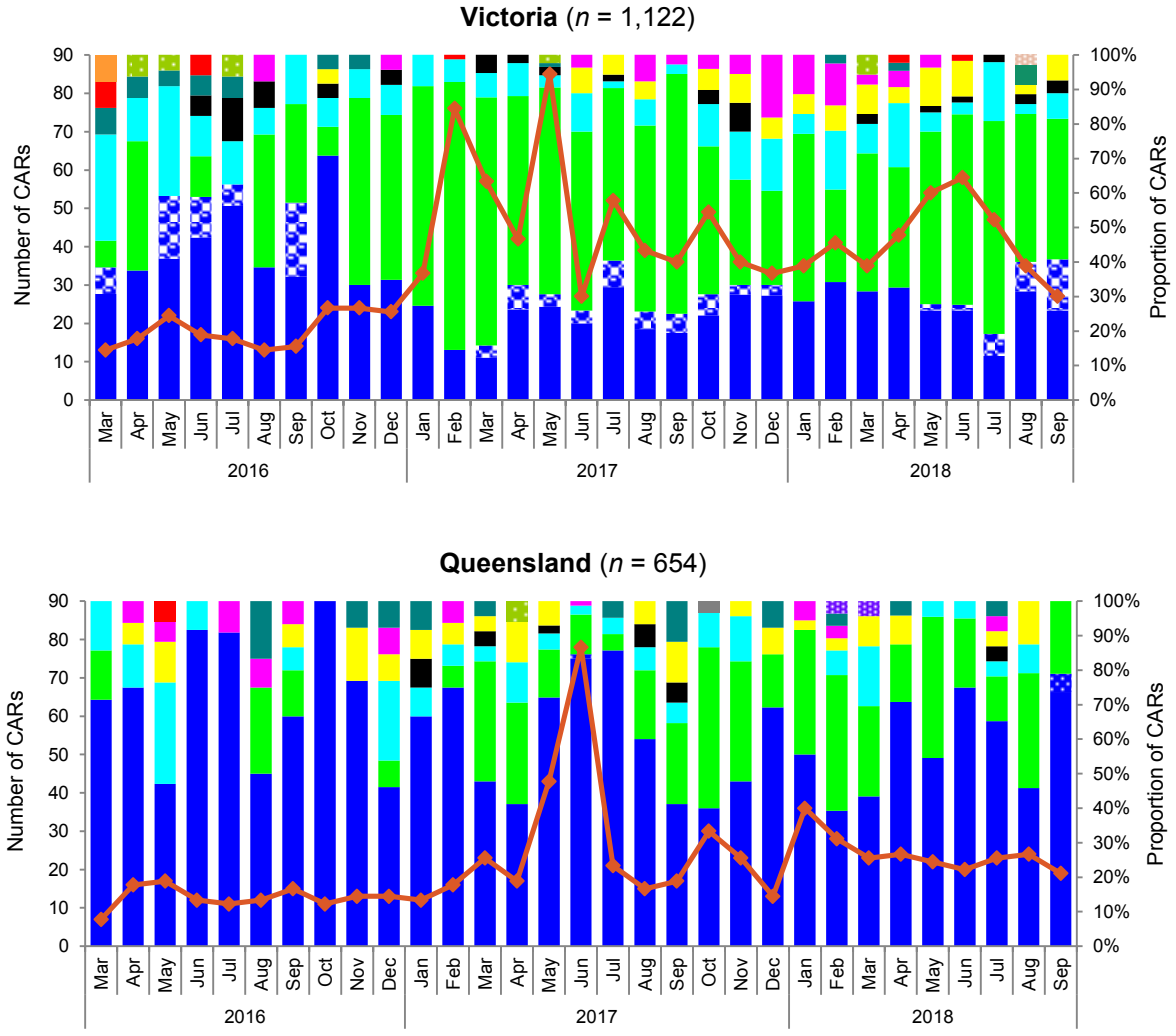
Figure 12. Critical antimicrobial resistances, number and distribution reported nationally, and by state and territory, 16 March 2016 to 30 September 2018



Lines represent the number of CARs reported each month; bars show the proportion of each CAR per month

- 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
- 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 (HLR) *Neisseria gonorrhoeae*
- Ceftriaxone non-susceptible and azithromycin non-susceptible (LLR) *Neisseria gonorrhoeae*

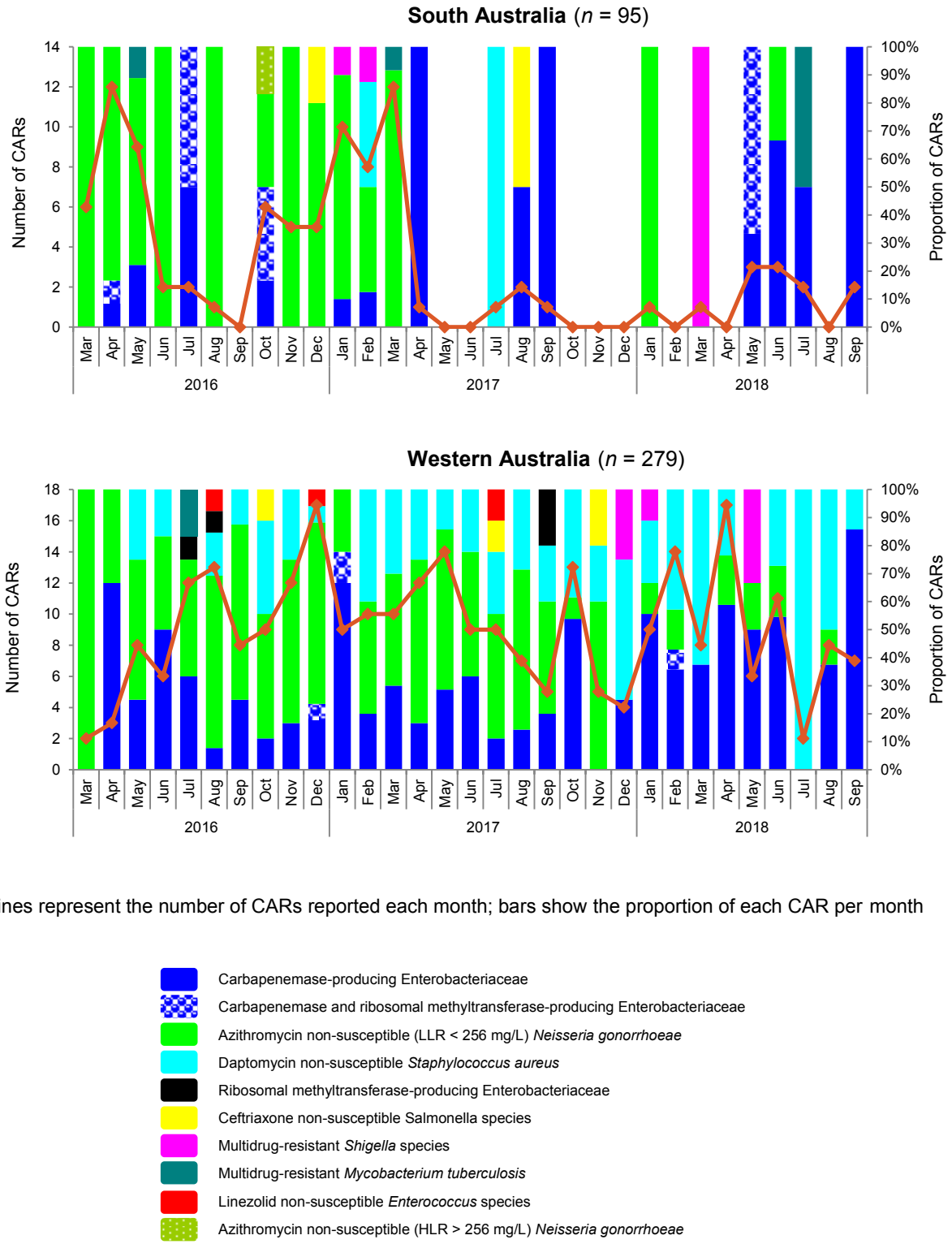
Figure 12 (continued). Critical antimicrobial resistances, number and distribution reported nationally, and by state and territory, 16 March 2016 to 30 September 2018



Lines represent the number of CARs reported each month; bars show the proportion of each CAR per month

- 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
- 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 (HLR) *Neisseria gonorrhoeae*
- Ceftriaxone non-susceptible and azithromycin non-susceptible (LLR) *Neisseria gonorrhoeae*

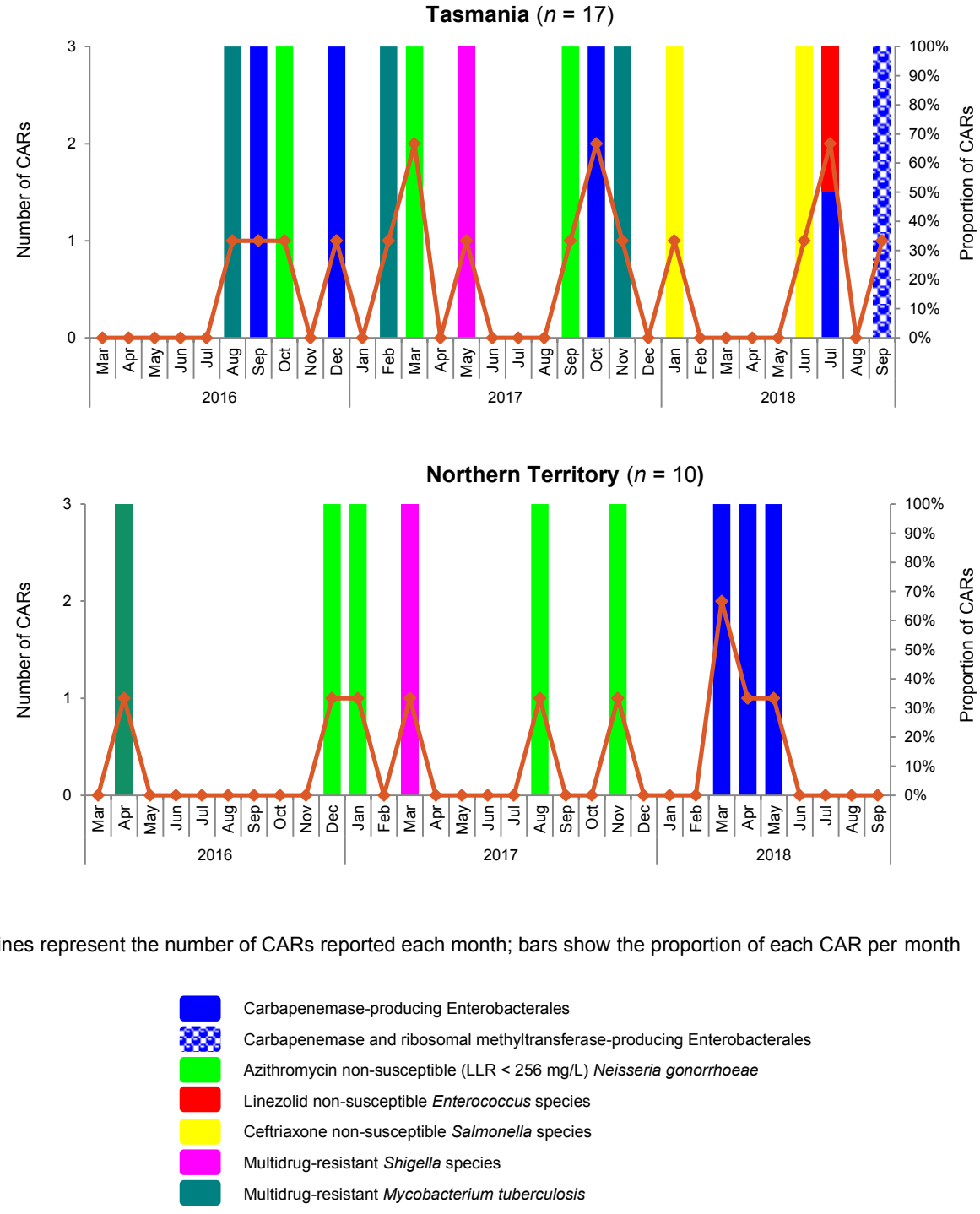
Figure 12 (continued). Critical antimicrobial resistances, number and distribution reported nationally, and by state and territory, 16 March 2016 to 30 September 2018



Lines represent the number of CARs reported each month; bars show the proportion of each CAR per month

- Carbapenemase-producing Enterobacteriaceae
- Carbapenemase and ribosomal methyltransferase-producing Enterobacteriaceae
- Azithromycin non-susceptible (LLR < 256 mg/L) *Neisseria gonorrhoeae*
- Daptomycin non-susceptible *Staphylococcus aureus*
- Ribosomal methyltransferase-producing Enterobacteriaceae
- 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*

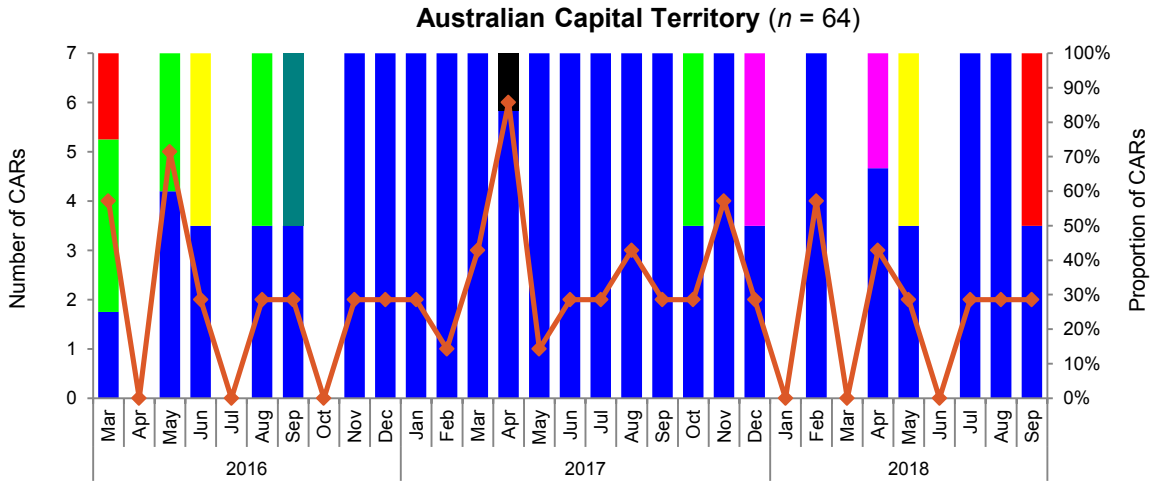
Figure 12 (continued). Critical antimicrobial resistances, number and distribution reported nationally, and by state and territory, 16 March 2016 to 30 September 2018



Lines represent the number of CARs reported each month; bars show the proportion of each CAR per month

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

Figure 12 (continued). Critical antimicrobial resistances, number and distribution reported nationally, and by state and territory, 16 March 2016 to 30 September 2018



Lines represent the number of CARs reported each month; bars show the proportion of each CAR per month

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

Conclusions

The establishment of CARAlert in 2016 was a significant enhancement to the AURA Surveillance System, which has provided timely national data on CARs to inform quality improvement initiatives and policies to reduce antimicrobial resistance. CARAlert complements systems in some states for monitoring selected CARs; these are not widespread. As at 30 September 2018, 93 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 continue to be dominated by those of the IMP type, found most often in the *E. cloacae* complex. IMP-producing Enterobacterales were reported in 50 hospitals; nine of which had more than five isolates reported during the six-month reporting period. NDM-producing Enterobacterales were reported from all states and territories. OXA-48-like organisms continue to rise.

The frequency of reporting of CPE highlights the importance of the implementation of the Commission's Recommendations for the control of carbapenemase-producing Enterobacterales: a guide for acute health facilities.[2]

The three *N. gonorrhoeae* with ceftriaxone non-susceptibility, one of which was also azithromycin low-level non-susceptible (MIC < 256 mg/L) that were reported, occur in the context of reports from five countries in 2017 and 2018 of *N. gonorrhoeae* strains with resistance to ceftriaxone, and global concerns regarding the ongoing efficacy of current recommended treatments.[4-6] In Australia, the recommended treatment for *N. gonorrhoeae* is ceftriaxone in conjunction with azithromycin; this regimen was introduced to limit further development of resistance to ceftriaxone.[6] Effective surveillance of *N. gonorrhoeae* AMR, continuation of sexually transmitted infection prevention and control programs, and outbreak response strategies are all key to minimising the spread of untreatable gonorrhoea.

The data on azithromycin non-susceptible and ceftriaxone non-susceptible *N. gonorrhoeae* reported to CARAlert complement the comprehensive long term Australian Gonococcal Surveillance Programme.[7] This 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 low background rate of azithromycin non-susceptible (low-level resistance) *N. gonorrhoeae* in Australia is now well established; reports of azithromycin non-susceptible *N. gonorrhoeae* (low-level resistance) remained steady from 1 April 2018 to 30 September 2018. The clinical implications of this low-level resistance are not clear. Ongoing monitoring of azithromycin and ceftriaxone non-susceptibility is required because of the importance of emerging changes in susceptibility for treatment guidelines.

Other CARs remain at very low levels, however ongoing prevention strategies and monitoring is essential to ensure that these CARs continue to remain low in Australia.

In 2018, in conjunction with relevant experts and the states and territories, the Commission completed a review of the resistances and species reported to CARAlert. From 2019, four new CARs will be reported to CARAlert. These are: transferrable resistance to colistin in Enterobacterales, carbapenemase-producing *Acinetobacter baumannii* complex, carbapenemase-producing *Pseudomonas aeruginosa* and *Candida auris*.

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.
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) *Neisseria gonorrhoeae*
AZI (LLR)	Azithromycin non-susceptible, low level resistance (LLR, MIC < 256 mg/L) *Neisseria gonorrhoeae*
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*

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