



**CARAlert**  
THE NATIONAL ALERT  
SYSTEM FOR CRITICAL  
ANTIMICROBIAL RESISTANCE



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## Introduction

The National Alert System for Critical Antimicrobial Resistances (CARAlert) was established in March 2016 as part of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System co-ordinated by the Australian Commission on Safety and Quality in Health Care (the Commission). CARAlert collects surveillance data on eight priority organisms with critical resistance to last-line antimicrobial agents.

Primary responsibility for clinical response to critical resistances lies with local health organisations and the state and territory health departments. The roles of CARAlert at the national level include collecting and analysing data to identify trends and timely communication of information concerning critical resistances to states and territories, to complement current local reporting of results. It is intended that states and territories will use the data to identify local problems, and respond to potential and proven multi-site outbreaks of CARs.

Over time, the data will increasingly be useful to inform safety and quality improvement programs.

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. CARs have been detected across Australia; they can result in significant morbidity and mortality in healthcare facilities, and in the community.

The CARs included in the CARAlert system 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<sup>1</sup>. The scope of organisms and CARs will be regularly reviewed, based on the latest available evidence on critical resistances which emerge in Australia and overseas.

**Table 1 – Critical Antimicrobial Resistances reported to CARAlert**

Species	Critical Resistance
<b><i>Enterobacteriaceae</i></b>	Carbapenemase-producing strains, or Ribosomal methylase-producing strains
<b><i>Enterococcus</i> species</b>	Linezolid non-susceptible
<b><i>Mycobacterium tuberculosis</i></b>	Multidrug-resistant (MDR) – at least rifampicin and isoniazid-resistant – strains
<b><i>Neisseria gonorrhoeae</i></b>	Ceftriaxone non-susceptible or azithromycin-resistant strains
<b><i>Salmonella</i> species</b>	Ceftriaxone non-susceptible strains
<b><i>Shigella</i> species</b>	MDR strains
<b><i>Staphylococcus aureus</i></b>	Vancomycin, linezolid or daptomycin non-susceptible
<b><i>Streptococcus pyogenes</i></b>	Penicillin reduced susceptibility

Under existing testing processes, originating laboratories undertake routine tests of an isolate to identify whether it is potentially a CAR; if suspected as a CAR, the isolate is referred to a confirming laboratory.

The confirming laboratory advises the originating laboratory of the result of the test for reporting back to the general practice or hospital that cared for the patient from whom the specimen was collected. The reports occur before the confirming laboratory enters the details of the resistance and organism into the CARAlert web portal. Alerts are reported to the Commission and to nominated state and territory health personnel weekly.

<sup>1</sup> Australian Commission on Safety and Quality in Health Care (ACSQHC). *AURA 2016: first Australian report on antimicrobial use and resistance in human health*. Sydney: ACSQHC 2016.

There are 28 confirming laboratories currently participating in CARAlert.

The data in this report are based on the date that the CAR was confirmed. The majority of CARs are submitted within seven days of confirmation. However, some batch testing occurs for isolates referred to the National Neisseria Network (NNN) and the Australian Mycobacterium Reference Laboratory Network (AMRLN) laboratories. This may result in the outcome of testing being entered into the CARAlert database in the following month.

This report includes CARs submitted between 17 March 2016 and 31 October 2016, and complements the individual alerts sent to the nominated state and territory contacts.

## Critical Antimicrobial Resistances

### Summary

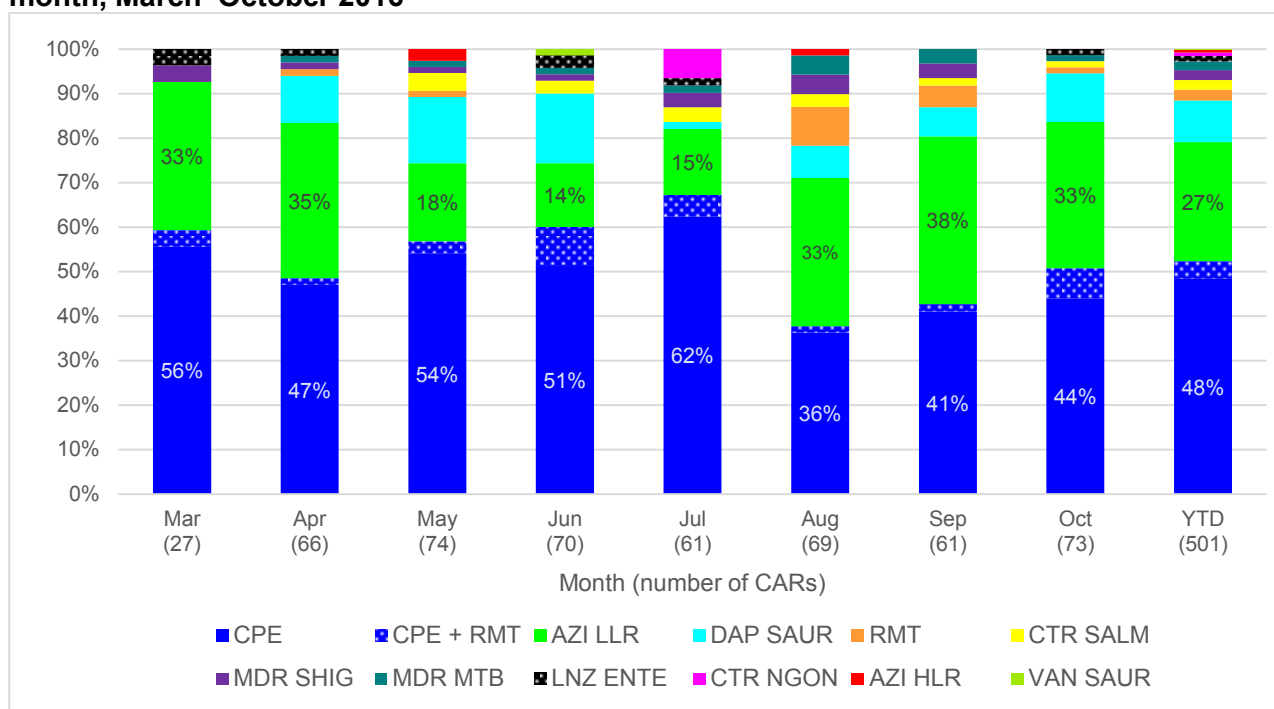
From 17 March 2016 to 31 October 2016 a total of 501 results were entered in the system, with an average of 67 per month from April to October (Figure 1). Isolates for these reports were referred from 62 originating laboratories across Australia. The proportion of CARs associated with priority organisms is shown in Figure 1. The number of CARs reported by species and month is shown in Figure 2.

Carbapenemase-resistant *Enterobacteriaceae* (CPE) were the most frequently recorded CAR of all CARs reported in the year to date (262, 52%), either alone (242, 48%), or in combination with ribosomal methylases (20, 4%). The differences in the proportion of CPE per month were not statistically significant ( $\chi^2$  for trend,  $p=0.1007$ ).

The next most frequently reported CAR was azithromycin-resistant *Neisseria gonorrhoeae* (137, 27%). Confirmation of this CAR is often performed in batches, which influences the numbers seen per month. Only three of the 137 (2.2%) azithromycin-resistant *N. gonorrhoeae* were reported to have high-level resistance (HLR) - i.e. minimum inhibitory concentration (MIC)  $\geq 256$  mg/L.

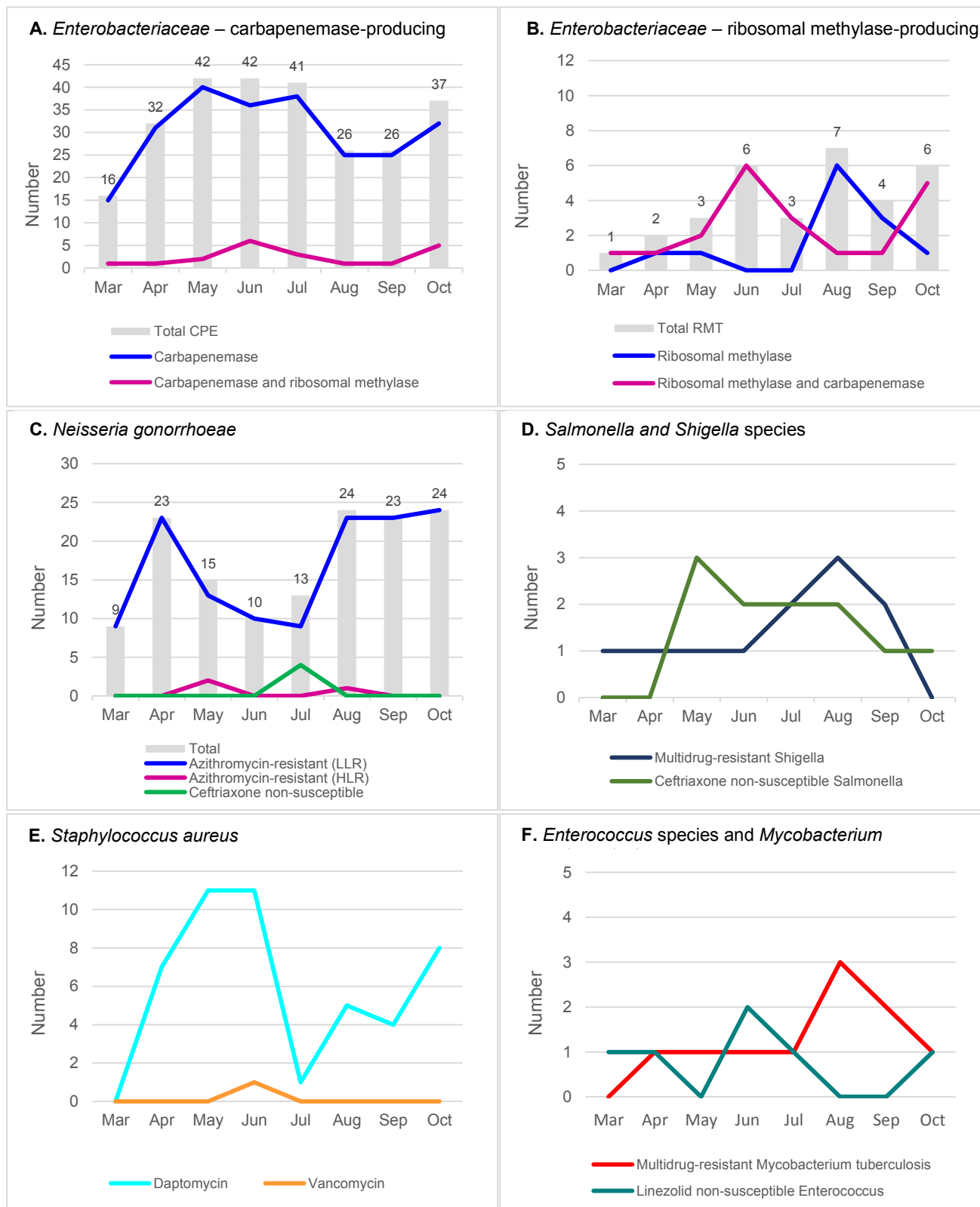
For the month of October, 73 new CAR records were entered. CPE continues to be the most frequently reported CAR (37, 51%), followed by azithromycin-resistant *N. gonorrhoeae* with low-level resistance (LLR) [MIC < 256 mg/L] (24, 33%) and daptomycin non-susceptible *S. aureus* (8, 11%).

**Figure 1: Critical antimicrobial resistances (CARs), as a percentage of all CARs, reported by month, March–October 2016**



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

**Figure 2: Critical antimicrobial resistances, number reported by species and month, March–October 2016**



### Critical Antimicrobial Resistances by state and territory

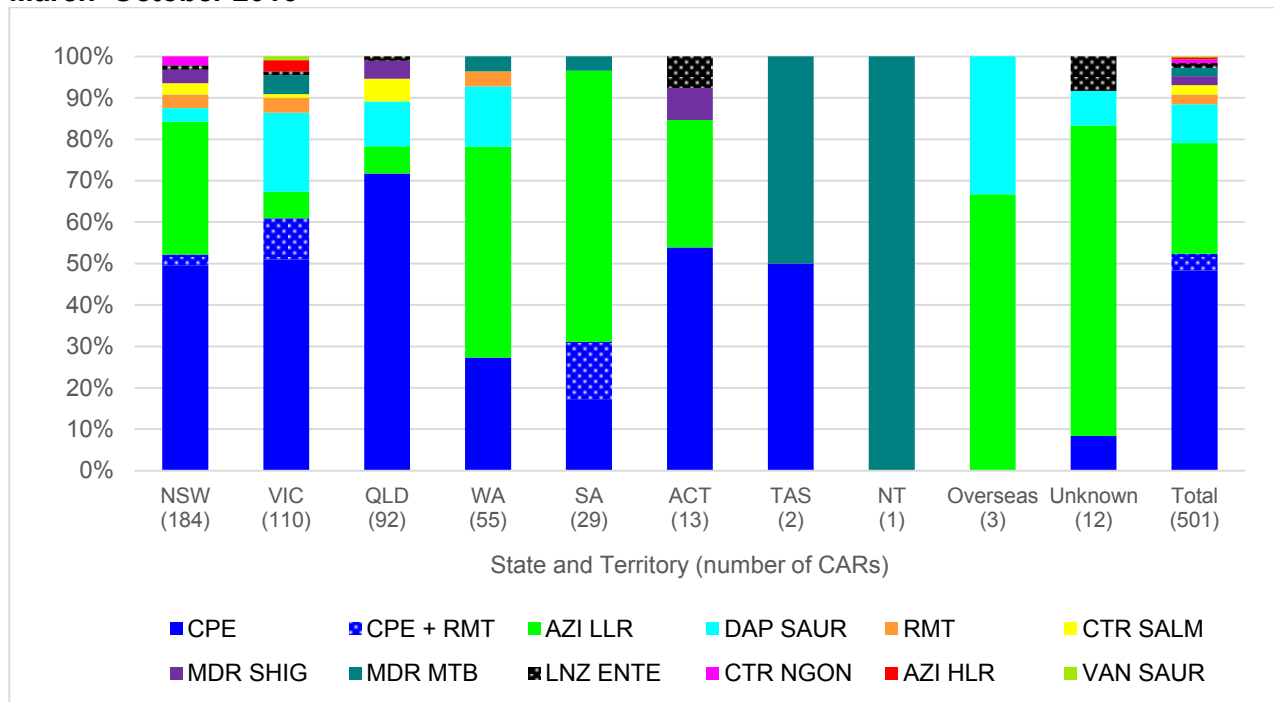
Seventy-seven per cent of all CARs were from the three most populous states: New South Wales (37%), Victoria (22%) and Queensland (18%). One report was received from the Northern Territory and two from Tasmania. Almost half (48%) of all CARs submitted were for CPE. Low prevalence of CPE was reported from South Australia (17%) and Western Australia (24%), with Queensland (72%) reporting the highest prevalence (Figure 3).

There were a significant number of entries of azithromycin-resistant (low-level resistance [LLR] MIC < 256 mg/L) *N. gonorrhoeae* from South Australia in March. As batch testing of this CAR is common, reports were analysed by date of collection, rather than date of confirmation (Figure 4). There were isolates from South Australia collected in January with LLR, and only small numbers of strains were confirmed with a collection date after April. There was a sharp increase in reports of this CAR in April from New South Wales, with a peak during July. Ceftriaxone non-susceptible strains collected in July were also confirmed from New South Wales. Western Australia has also seen a significant increase in the number of LLR strains. Three strains with high-level azithromycin resistance (MIC ≥ 256 mg/L) were confirmed in Victoria, one each collected in April, May, and July.

State or territory of residence was not available for 15 reports (nine azithromycin-resistant [LLR] MIC < 256 mg/L] *N. gonorrhoeae*, four CPE, and one each of linezolid non-susceptible *Enterococcus* species and daptomycin non-susceptible *S. aureus*). For *N. gonorrhoeae*, this is due to the isolates being collected from patients that attended sexual health clinics, where postcode of residence is not sought. Three reports were from overseas residents, one daptomycin non-susceptible *S. aureus*, and two azithromycin-resistant (LLR, MIC < 256 mg/L) *N. gonorrhoeae*.

Daptomycin non-susceptible *S. aureus* were reported from four states/territories, with 47% (21/45) from Victoria and 18% (8/45) from Western Australia. Multidrug-resistant (MDR) *Mycobacterium tuberculosis* were reported from patients from five state/territories.

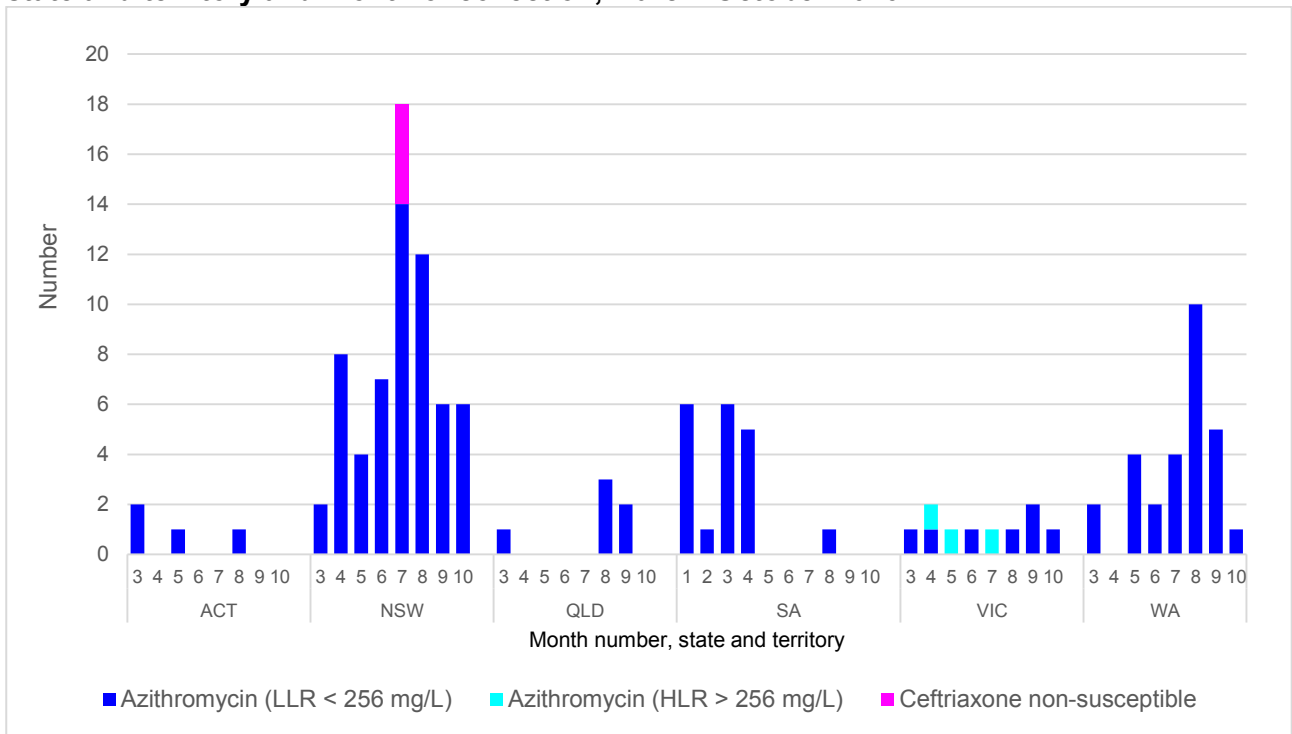
**Figure 3: Critical antimicrobial resistances, percentage reported by state and territory, March–October 2016**



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



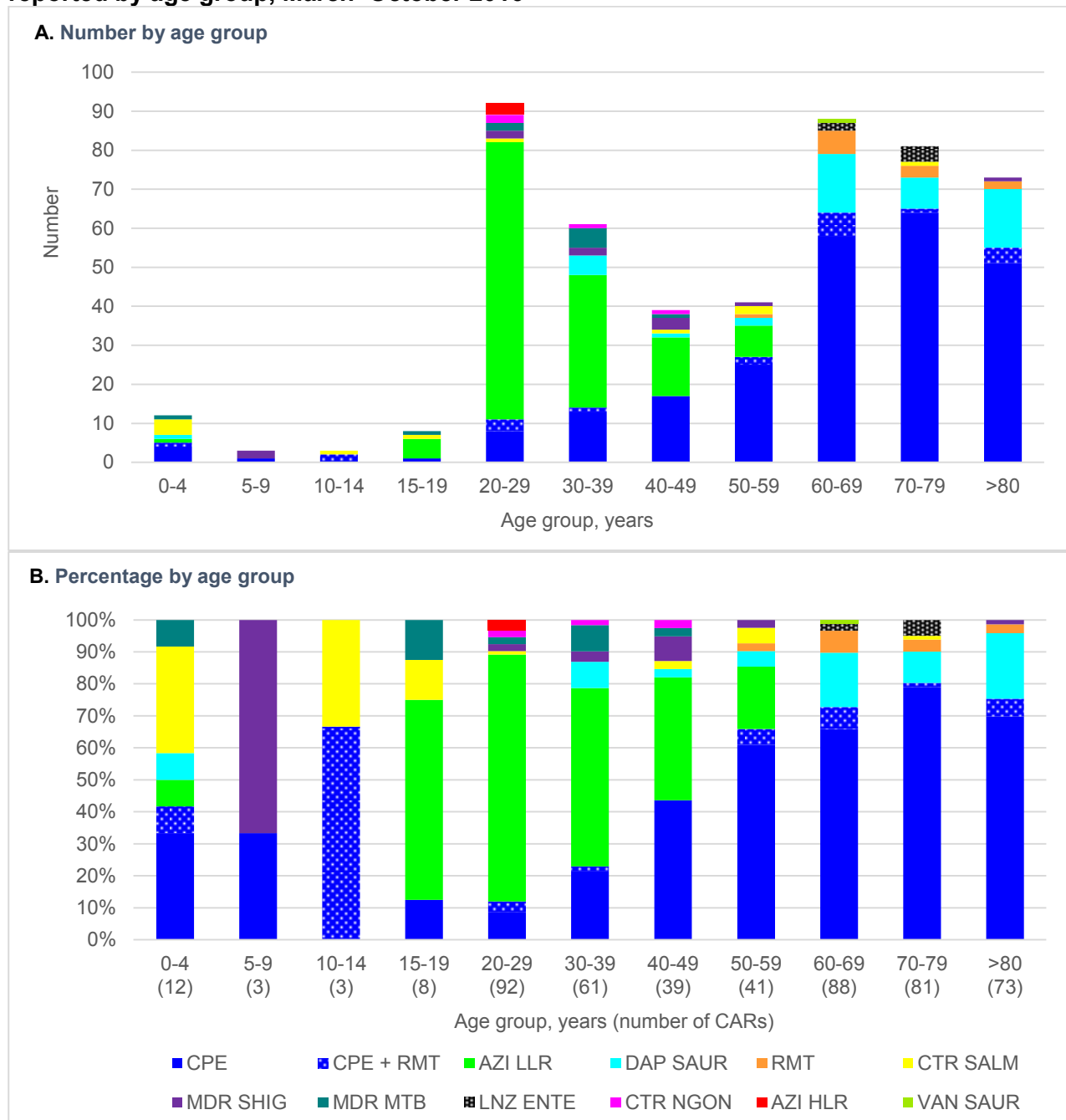
**Figure 4: Critical antimicrobial resistances, *Neisseria gonorrhoeae*, number reported by state and territory and month of collection, March–October 2016**



## Critical Antimicrobial Resistances by age group

Seventy per cent (184/262) of CPE were from people aged 60 years and older, the age range was from 0-4 to >80 years; with a median age of 60-69 years (see Figure 5). Azithromycin-resistant *N. gonorrhoeae* were the predominant CAR reported among 15-19, 20-29 and 30-39 years age groups. Only 3.6% (18/501) of all CARs were reported in children aged less than 15 years; CPE and ceftriaxone non-susceptible *Salmonella* species were common (72%).

**Figure 5: Proportion of critical antimicrobial resistances, number (A) and percentage (B) reported by age group, March–October 2016**



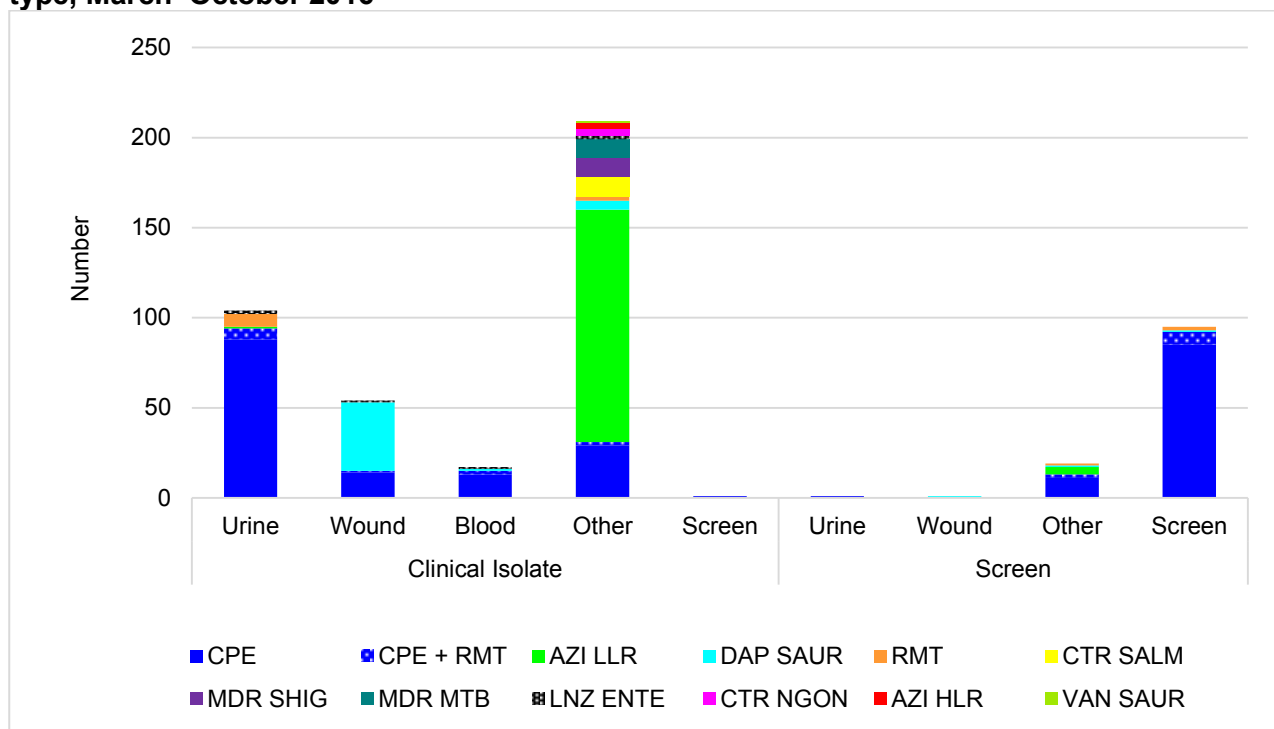
CPE = carbapenemase-producing-*Enterobacteriaceae*; RMT = ribosomal methylase-producing *Enterobacteriaceae*; CPE+RMT = carbapenemase- and ribosomal methylase-producing *Enterobacteriaceae*; LNZ ENTE = linezolid non-susceptible *Enterococcus* species; AZI (LLR) = azithromycin-resistant (LLR, MIC < 256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

## Critical Antimicrobial Resistances by specimen type

Over 76% of all CARs were from clinical specimens (specimens collected for diagnostic purposes, as opposed to those taken for screening). These include urine, wound, blood and other (e.g. genital or respiratory) specimens (Figure 6).

Sixty per cent (156/262) of CPE isolates were from clinical specimens, with 60% (94/156) of these from urine, and 10% (15/156) from blood cultures. One linezolid non-susceptible *E. faecalis* and one daptomycin non-susceptible *S. aureus* were from blood culture. Urine is an important specimen for certain CARs such as CPE and the urinary tract is a common site of infection.

**Figure 6: Critical antimicrobial resistances by specimen type, number reported by specimen type, March–October 2016**



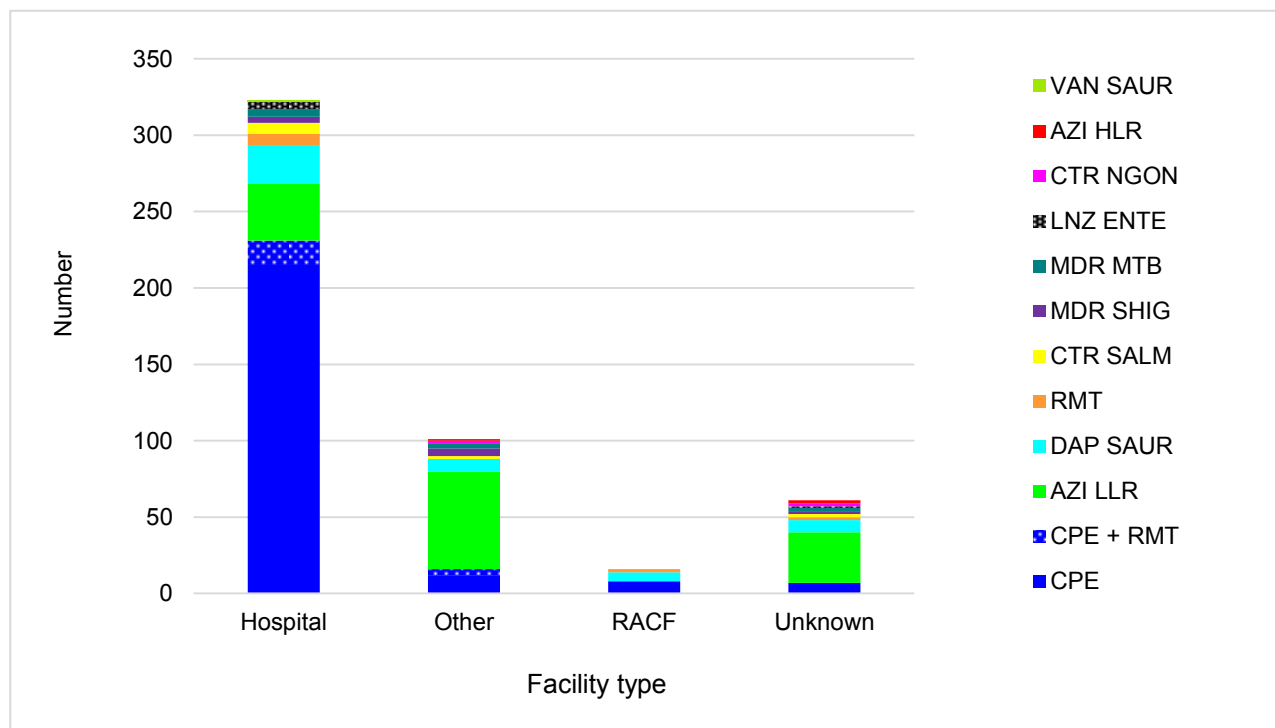
Other specimen type: Not-urine, wound, or blood (e.g. genital, faecal, respiratory)

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

## Critical Antimicrobial Resistances by facility type

While most CARs were detected in either hospitalised patients or hospital outpatients (64%, 323/501), some were found in the community (20%, 101/501) and in residential aged-care facilities (Figure 7). Facility type for azithromycin-resistant *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 7: Critical antimicrobial resistances, number reported by facility type, March–October 2016**



Other: Community (non-hospital and non-residential aged care facility)

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

## Carbapenemase-producing *Enterobacteriaceae* type by state and territory

There were significant regional differences noted in the carbapenemase types detected throughout Australia. NDM in association with OXA-48-like types were reported from Victoria, New South Wales and South Australia, as shown in Figure 8.

Two carbapenemase types, IMP (62%, 163/262) and NDM (21%, 55/262), accounted for 83% (218/262) of all *Enterobacteriaceae* with a confirmed carbapenemase. Six different types (IMP, NDM, OXA-48-like, KPC, VIM, and SME) were reported.

IMP-type carbapenemases comprised the majority (>70%) of CPE in New South Wales (81%, 78/96), Queensland (88%, 58/66) and the Australian Capital Territory (71%, 5/7). No IMP-producing *Enterobacteriaceae* were reported from South Australia or Tasmania. Only the bla<sub>IMP-4</sub> strain has been identified in genetic sequencing to date (38%, 62/163).

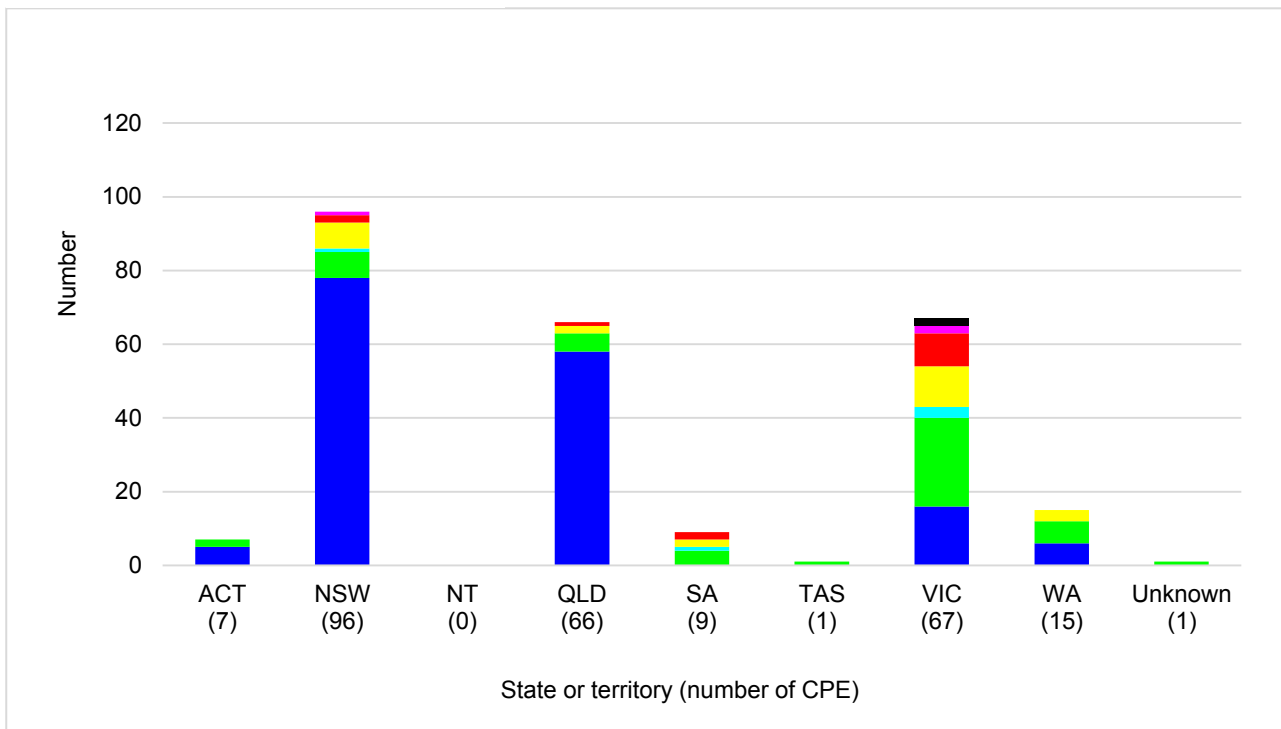
NDM types were found in all states and territories where CPE were detected. NDM types contributed to 40% (27/67) of all types found in Victoria. NDM and /or NDM+OXA-48-like types were also common in South Australia (55%, 5/9). Four different genes were found in the strains sequenced to date: bla<sub>NDM-5</sub> (44%, 14/32), bla<sub>NDM-1</sub> (34%, 11/32), bla<sub>NDM-4</sub> (13%, 4/32), and bla<sub>NDM-7</sub> (9%, 3/32). Ribosomal methylases were often detected among isolates containing NDM types (32.7%, 18/55; rmtB [13], armA [3], rmtB+rmtF [1] and rmtB+rmtE [1]).

*Klebsiella pneumoniae* carbapenemase (KPC) types were mostly confined to Victoria (13%, 9/67), although reports were noted in three other states (New South Wales and South Australia, n=2 each; and Queensland, n=1).

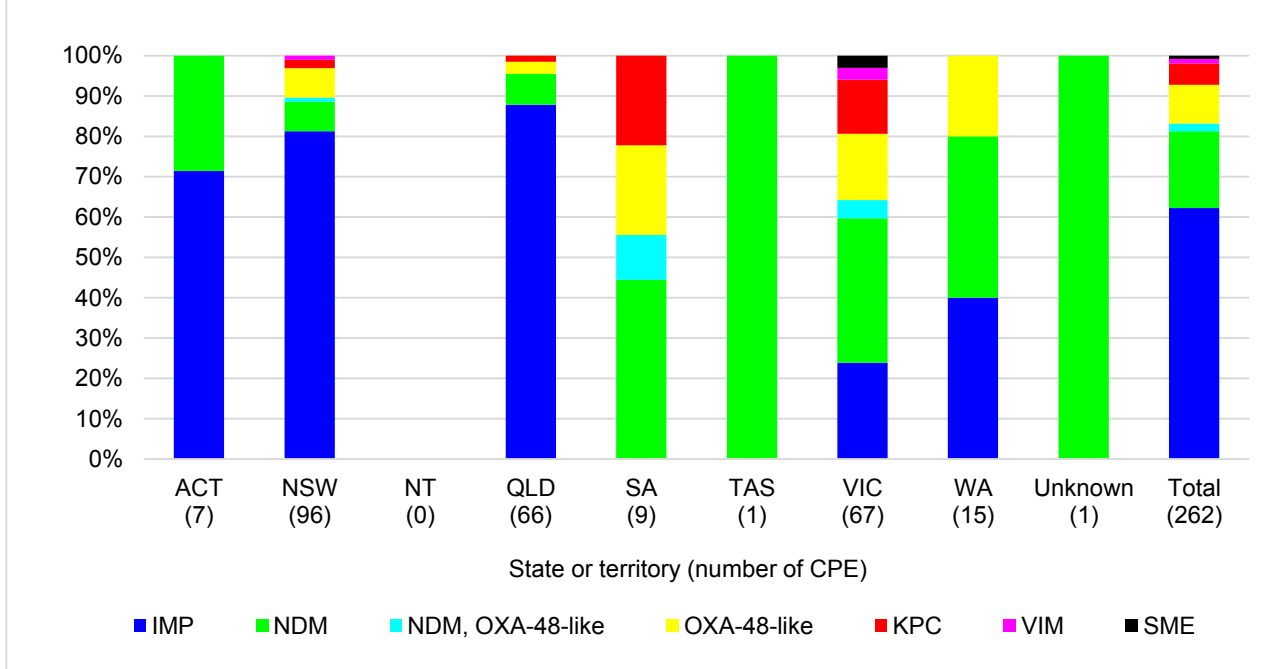
No CPE have been reported from the Northern Territory to date.

**Figure 8: Carbapenemase types as a proportion of all carbapenemases, number (A) and percentage (B) reported by state and territory, March–October 2016**

**A. Number by state and territory**

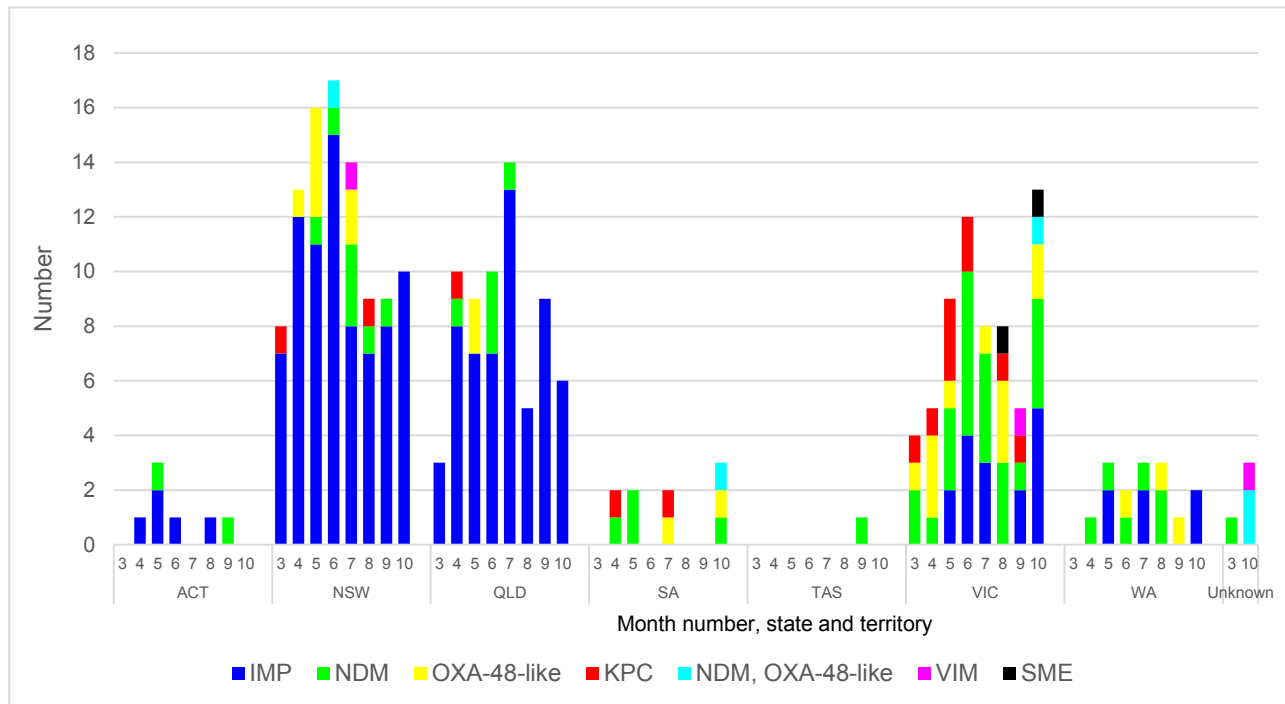


**B. Percentage by state and territory**



The distribution of carbapenemase types by state and territory and month of confirmation is shown in Figure 9. There was a peak in reports during June and July in New South Wales, Queensland and Victoria. The sharp increase noted in October for Victoria reflects several isolates that were collected in September. Of interest is the emergence of two *Serratia marcescens* with SME type in Victoria. There have been increasing numbers of SME carbapenemases reported globally especially in the Americas. It is a signal of potential emerging resistance that may have implications for selection of treatments.

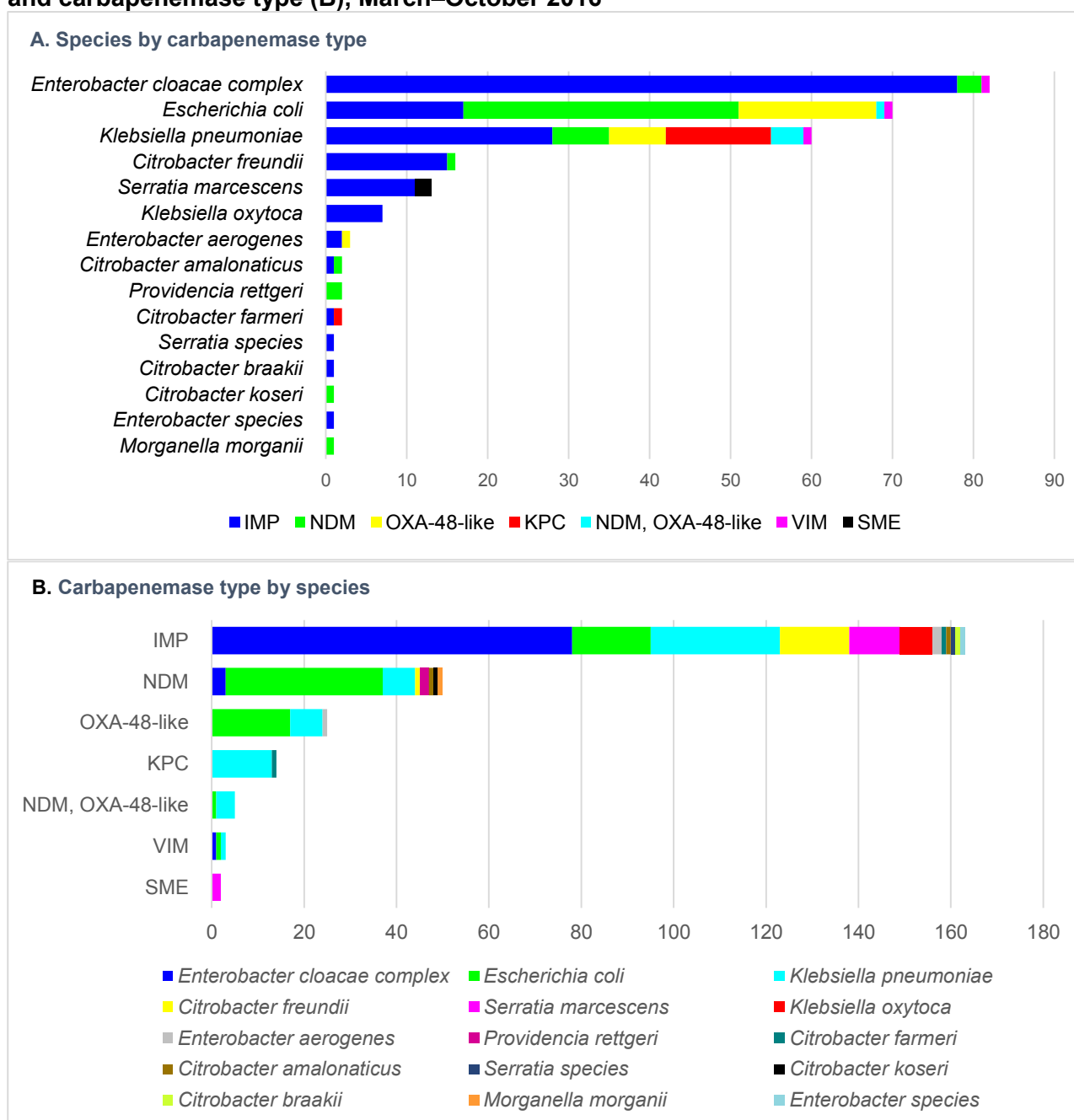
**Figure 9: Carbapenemase types, number reported by month and state and territory, March–October 2016**



## Organism by Carbapenemase-producing *Enterobacteriaceae* type

Carbapenemases were found in 15 species of *Enterobacteriaceae*. IMP-type carbapenemase accounted for 62% (163/262) of all carbapenemases, and was found in 12 different species (Figure 10). *Enterobacter cloacae* complex accounted for 48% (78/163) of all IMP-type carbapenemases and 31% (82/262) of all CPE. However, in Queensland 58% (38/66) of all CPE reported were *E. cloacae* complex containing IMP types. NDM and OXA-48-like carbapenemase types were found mainly in *E. coli* (68%, 34/50; 68%, 17/25, respectively); however, when both NDM and OXA-48-like types were found together, they were mainly in *K. pneumoniae* (80%, 4/5). One KPC (7%, 1/14) was found in *Citrobacter farmeri*.

**Figure 10: Carbapenemase-producing Enterobacteriaceae, number reported by species (A) and carbapenemase type (B), March–October 2016**





### Other Critical Antimicrobial Resistance types

Ceftriaxone non-susceptible *N. gonorrhoeae* were reported from NSW, and contributed to 31% (4/13) of all *N. gonorrhoeae* in July.

For *S. aureus*, 98% were daptomycin non-susceptible strains (47/48). One vancomycin non-susceptible (vancomycin intermediate) strain was reported in June from Victoria. No linezolid non-susceptible *S. aureus* strains were reported.

Ribosomal methylases were detected in 32 *Enterobacteriaceae*, representing seven different species, 63% (20/32) of which also had a carbapenemase. Ribosomal methylases are not always associated with a carbapenemase gene. Five genes were found: *rmtB* (63%, 20/32), *armA* (25%, 8/32), *rmtC* (9%, 3/32), *rmtF* (3%, 1/32). Two isolates had multiple genes: *Providencia rettgeri* (*rmtB*, *rmtE*, and NDM) and *K. pneumoniae* (*rmtB*, *rmtF*, and NDM+OXA-48-like).

## Conclusion

For this reporting period, 62 originating laboratories contributed CARs to 28 confirming laboratories. All states and territories have had at least one CAR reported.

The Commission will continue to monitor records from the CARAlert System, and prepare summary reports on a regular basis. The volume of CARs will continue to be monitored to inform frequency of reports. The Commission will provide ad hoc reports to the nominated jurisdictional contacts, as required.

The relatively small number of records in the database to date means that it is not possible to draw conclusions or learnings from the analyses. As the data collection develops and numbers of reports increase sufficiently to enable meaningful analyses of trends and their implications, it is anticipated that the data will increasingly inform safety and quality improvement initiatives and antimicrobial resistance reduction policies.

A review of CARAlert was conducted during October 2016 by the Commission; the results are currently being analysed. Refinements may be made to the process of alerts and reporting following consideration of feedback provided as part of the review and the findings outlined in this report.

Enquiries regarding either this Report or the CARAlert System may be submitted to [CARAlert@safetyandquality.gov.au](mailto: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: <ul style="list-style-type: none"> <li>notify the originating laboratory of test outcomes through the usual communication channels, regardless of whether a CAR is confirmed or not.</li> <li>enter data for each confirmed CAR into the CARAlert web-portal.</li> </ul> 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. <p>If an originating laboratory identifies an isolate that may have the potential to be a CAR, it:</p> <ul style="list-style-type: none"> <li>notifies the requesting clinician of the test results, and the suspected CAR</li> <li>sends the suspected isolate onto a confirming laboratory for confirmation.</li> </ul>
Abbreviation	Critical antimicrobial resistance
CPE	carbapenemase-producing <i>Enterobacteriaceae</i>
RMT	ribosomal methylase-producing <i>Enterobacteriaceae</i>
CPE+RMT	carbapenemase- and ribosomal methylase-producing <i>Enterobacteriaceae</i>
LNZ ENTE	linezolid non-susceptible <i>Enterococcus</i> species
AZI (LLR)	Azithromycin-resistant (LLR, MIC < 256 mg/L) <i>Neisseria gonorrhoeae</i>
AZI (HLR)	Azithromycin-resistant (HLR, MIC > 256 mg/L) <i>Neisseria gonorrhoeae</i>
CTR NGON	ceftriaxone non-susceptible <i>Neisseria gonorrhoeae</i>
DAP SAUR	daptomycin non-susceptible <i>Staphylococcus aureus</i>
VAN SAUR	vancomycin non-susceptible <i>Staphylococcus aureus</i>
CTR SALM	ceftriaxone non-susceptible <i>Salmonella</i> species
MDR SHIG	multidrug-resistant <i>Shigella</i> species
MDR MTB	multidrug-resistant <i>Mycobacterium tuberculosis</i>