

AUSTRALIAN COMMISSION
ON SAFETY AND QUALITY IN HEALTH CARE



AURA 2017

Second Australian report on antimicrobial use
and resistance in human health

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Contents

Summary	v
Chapter 1: Introduction	1
Key messages	1
1.1 Background	2
1.2 Australian healthcare system context	4
1.3 Importance of antimicrobial resistance	6
1.4 Importance of surveillance	7
1.5 AURA 2017 report	10
Chapter 2: Data sources and methods	13
Key messages	13
2.1 Types of data and information collected under the Antimicrobial Use and Resistance in Australia Surveillance System	14
2.2 Sources of data for antimicrobial use and appropriateness of prescribing	14
2.3 Sources of data for antimicrobial resistance	15
2.4 Considerations for interpreting the data	19
2.5 Data governance processes	20
Chapter 3: Antimicrobial use and appropriateness	23
Key messages	23
3.1 Antimicrobial use in hospitals	24
3.2 Antimicrobial use in the community - primary care	61
3.3 Developments and future plans	79
Chapter 4: Antimicrobial resistance	87
Key messages	87
4.1 Introduction	88
4.2 <i>Acinetobacter baumannii</i> complex	95
4.3 Enterobacteriaceae	97
4.4 <i>Enterococcus</i> species	110
4.5 <i>Mycobacterium tuberculosis</i>	116
4.6 <i>Neisseria gonorrhoeae</i>	119
4.7 <i>Neisseria meningitidis</i>	122
4.8 <i>Pseudomonas aeruginosa</i>	125
4.9 <i>Salmonella</i> species	127
4.10 <i>Shigella</i> species	129



4.11	<i>Staphylococcus aureus</i>	130
4.12	<i>Streptococcus agalactiae</i>	138
4.13	<i>Streptococcus pneumoniae</i>	139
4.14	<i>Streptococcus pyogenes</i>	141
Chapter 5: National Alert System for Critical Antimicrobial Resistances (CARAlert)		145
	Key messages	145
5.1	Overview of the CARAlert system	146
5.2	Results from CARAlert 2016	148
5.3	Conclusion	160
Chapter 6: Focus areas		165
	Key messages	165
6.1	The growing problem of vancomycin-resistant enterococci	166
6.2	The Queensland clone of CA-MRSA: a homegrown and increasing problem	168
6.3	International comparisons	170
6.4	Standardising Australia's approach to susceptibility testing	181
Chapter 7: Conclusions and future developments		185
	Key messages	185
7.1	Lessons from AURA 2017	186
7.2	Next steps for the AURA Surveillance System	188
7.3	Future AURA reports	189
Appendix 1: Data source description		191
A1.1	Antimicrobial use collections	191
A1.2	Antimicrobial resistance collections	196
Appendix 2: Priority organisms		201
Appendix 3: Terminology		203
A3.1	Acronyms	203
A3.2	Common terms	204
References		207

Summary

AURA 2017: Second Australian report on antimicrobial use and resistance in human health provides data and analysis from the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System, primarily from 2015.

AURA 2017 includes data about organisms that have been determined to be a priority for Australia, the volume of antimicrobial use (AU), the appropriateness of antimicrobial prescribing, key emerging issues for antimicrobial resistance (AMR), and a comparison of Australia's situation with other countries.

This second AURA report provides an expanded view of AMR, AU and appropriateness of prescribing in Australia. Participation in the AURA Surveillance System by both public and private healthcare providers has grown, and the increased volume of data has greatly contributed to the capacity to use the AURA Surveillance System to identify emerging issues and monitor trends. AURA now includes the National Alert System for Critical Antimicrobial Resistances (CARAlert), which allows the early detection of critical antimicrobial resistances and, over time, will provide information on the effectiveness of measures to promote appropriate AU and contain AMR.

Key issues identified in AURA 2017 relating to antimicrobial use and appropriateness of prescribing

- Australia's antibacterial use in hospitals peaked in 2010, and has decreased by 9.2% between 2010 and 2015.
- Fluoroquinolone usage rates reduced in line with strategies to restrict use in most Australian hospitals.
- In hospitals, 23.3% of prescribing did not comply with guidelines, and 21.9% of prescriptions were assessed as inappropriate. Of surgical prophylaxis prescriptions, 27.4% were continued for longer than 24 hours (less than 5% is considered best practice).
- The most common reasons that hospital prescriptions were deemed to be inappropriate were:
 - an antimicrobial was not needed (19.6%) -
 - the antimicrobial chosen was incorrect (spectrum too broad: 25.2%)
 - the duration of treatment (17.7%) or the dose was incorrect (19.5%).
- More than 30 million antimicrobial prescriptions were dispensed through the Pharmaceutical Benefits Scheme/Repatriation Pharmaceutical Benefits Scheme in 2015. There has been little change in this number since 2008.
- Prescribing of antimicrobials to treat respiratory tract infections is common - more than 60% of patients with these conditions are prescribed an antimicrobial, but antimicrobials are usually not recommended for these conditions.

Key issues identified in AURA 2017 relating to antimicrobial resistance

- Compared with 2014, there were increases in rates of fluoroquinolone resistance in *Escherichia coli* from blood cultures (+2.5%) and *Shigella sonnei* (+10.9%).
- Among gram-negative bacteria, rates of resistance in the community remain relatively stable compared with 2014, and are low by world standards.
- Between March and December 2016, 673 results were submitted to CARAlert. Carbapenemase-producing Enterobacteriaceae was the most frequently recorded critical antimicrobial resistance (48%).
- The IMP-type carbapenemase is now endemic on the Australian eastern seaboard in multiple species of Enterobacteriaceae, but there is no evidence that other carbapenemases have become established in Australia.
- Vancomycin-resistant enterococci (VRE) have emerged as a major healthcare problem in Australia. When enterococci are resistant to vancomycin, only two or three reserved antimicrobials can be used to treat serious infections.
- The proportion of vancomycin-resistant *Enterococcus faecium* isolates in Australia increased rapidly from 2005, and is now higher than that in any European country. Reversing the incidence of VRE in Australia will be extremely challenging.
- The Queensland clone of methicillin-resistant *Staphylococcus aureus* (MRSA) has become the dominant community-associated MRSA (CA-MRSA) clone in Australia. CA-MRSA is now a more common cause of bloodstream infection than healthcare-associated MRSA.
- Community-onset infections caused by strains of MRSA are therefore likely to fail treatment with the usual β -lactams used by community practitioners, resulting in hospitalisation for

treatment with parenteral antimicrobials. This means that more patients will be treated with vancomycin and related agents, generating increasing selection pressure for other multidrug-resistant pathogens such as VRE.

- A challenge for health care is that, so far, no country has found effective interventions to control the spread of CA-MRSA; effort in this area is a priority.

In its second year of operation, AURA is providing a greater breadth and diversity of critical information needed by clinicians, policy makers, researchers and health system managers to inform antimicrobial stewardship and AMR policy and program development. Clinicians have advised the AURA National Coordination Unit (ANCU) at the Australian Commission on Safety and Quality in Health Care (the Commission) that AURA expands coverage and improves representativeness of both AMR and AU data, and that the data are actively being used to inform decisions about patient care.

AURA 2017 also highlights areas where future work will inform action to improve the use of antimicrobials and prevent the spread of AMR.

What is antimicrobial resistance?

AMR continues to be an issue of significant importance for health care in Australia, and globally. AMR occurs when bacteria change to protect themselves from the effects of antimicrobials. This means that the antimicrobial can no longer eradicate or stop the growth of the bacteria. Sometimes antimicrobials are prescribed inappropriately, such as when antibacterials are used to treat a viral infection, or antimicrobials are prescribed either when they are not indicated or for longer than necessary. Antimicrobials can be lifesaving agents in the fight against infection, but their effectiveness is diminished by inappropriate use and increasing AMR.

AMR has a direct effect on patient care and patient outcomes. It increases the complexity

Areas for action

Intensify efforts to reduce unnecessary prescribing in the community

Australia continues to have very high overall rates of community antimicrobial use compared with a number of comparable countries. In 2015, around half of the Australian population (44.7%, about 10.7 million people) had at least one antimicrobial dispensed under the Pharmaceutical Benefits Scheme (PBS) or the Repatriation Pharmaceutical Benefits Scheme (RPBS). Many antimicrobial prescriptions in the community are unnecessary because antimicrobials are frequently used to treat infections for which they provide little or no benefit.

AURA 2017 supports the recommendations of the *Australian Atlas of Healthcare Variation* with regard to antimicrobial dispensing, and the Antimicrobial Stewardship Clinical Care Standard. These include national benchmarks for prescribing of antimicrobials, examination by the Pharmaceutical Benefits Advisory Committee (PBAC) of use of amoxicillin-clavulanate, and implementation of antimicrobial stewardship programs in general practice to reduce the use of amoxicillin, amoxicillin-clavulanate and cefalexin.

The AURA National Coordination Unit (ANCU) will work with the Australian Government Department of Health to develop national benchmarks for best-practice prescribing of antimicrobial agents. The Australian Commission on Safety and Quality in Health Care (the Commission) will also work with the PBAC to examine appropriate access to amoxicillin-clavulanate on the PBS/RPBS, given that most prescribing of

this antimicrobial is for conditions that do not require an antimicrobial, or for which amoxicillin alone is recommended in national guidelines.

Implement actions to control carbapenemase-producing Enterobacteriaceae

Data from the National Alert System for Critical Antimicrobial Resistances (CARAlert) show that carbapenemase-producing Enterobacteriaceae were the most frequently recorded critical antimicrobial resistance between March and December 2016. The IMP-type carbapenemase is now endemic on the Australian eastern seaboard.

The Commission has published *Recommendations for the Control of Carbapenemase-producing Enterobacteriaceae (CPE): A guide for acute care health facilities* and will work with health service organisations to support timely implementation of these recommendations.

Monitor resistant gonococcal infections to inform treatment guidelines

CARAlert reports on isolates of *Neisseria gonorrhoeae* that are non-susceptible to ceftriaxone or azithromycin. Strains that are non-susceptible to azithromycin are more common than initially thought. CARAlert data complement state and territory systems that monitor antimicrobial resistance as part of prevention and control strategies for sexually transmissible infections. The emergence of antimicrobial-resistant *N. gonorrhoeae* at the same time as continued increases in disease notifications may lead to treatment failures and disease transmission.

continued

Areas for action: continued

Treatment guidelines for gonococcal infection should be reviewed in light of emerging non-susceptibility to azithromycin. The Commission will work with the states and territories to provide regular updates on ceftriaxone- or azithromycin-nonsusceptible *N. gonorrhoeae* through CARAlert, as well as to inform national and local treatment guidelines.

Strengthen infection control practices to minimise spread of vancomycin-resistant enterococci

Vancomycin-resistant enterococci are becoming a major healthcare problem in

Australia, and only two or three reserved antimicrobials can be used to treat serious infections. Strict adherence to infection control guidelines and effective cleaning and sterilisation in healthcare facilities is essential.

Improve the appropriateness of antimicrobial use for surgical prophylaxis

The use of antimicrobials for surgical prophylaxis is often suboptimal, and antimicrobials are often used for longer than necessary in this setting. The Commission will collaborate with the Royal Australasian College of Surgeons to progress guidance on antimicrobial use in surgical prophylaxis.

of treatment and the duration of hospital stay, resulting in additional burden to patients, clinicians and healthcare systems.

About the AURA Surveillance System

AURA has been developed in the context of One Health, which is a coordinated, collaborative, multidisciplinary and cross-sectoral approach to the development and implementation of health strategies for people, animals and the environment.

Surveillance is a critical element of Australia's National Antimicrobial Resistance Strategy and a priority for healthcare delivery for the states and territories and the private sector. In 2016, the Australian Government released an implementation plan to support the National Antimicrobial Resistance Strategy, which included surveillance as a key objective – AURA provides the human health elements of this surveillance. AURA also supports the National Safety and Quality Health Service Standards,

particularly the Preventing and Controlling Healthcare Associated Infection Standard.

AURA enables improved coordination and integration of data from a range of sources, and allows integrated analysis and reporting at a national level. The AURA Surveillance System was established based on a strategy of engagement with content experts in specialised fields where high-quality programs were in place, to more effectively bring together existing and new surveillance in an integrated way. This approach reduced duplication of effort, maximised existing expertise, and enabled a focus on enhancing surveillance.

Data for AURA are derived from and analysed by the ANCU and AURA program partners. New components of the surveillance system have also been developed to ensure a more comprehensive and coordinated approach.

Antimicrobial use and appropriateness of prescribing: key findings

AU continues to be a key driver of AMR – the more we use antimicrobials, the more likely it is that resistance will develop and spread. Appropriate use of antimicrobials can be lifesaving, but inappropriate use needs to be closely monitored and acted on to promote improved safety and quality of care. Examples of inappropriate use include prescribing antimicrobials when they are not necessary, prescribing the wrong type of antimicrobial and prescribing for the incorrect duration. These issues apply across the acute care and community sectors – Chapter 3 of AURA 2017 provides extensive data on AU and appropriateness of prescribing from both the public and private sectors.

Antimicrobial use in hospitals

Data on AU in hospitals have been drawn from the 2015 National Antimicrobial Utilisation Surveillance Program (NAUSP) report and from additional analyses to inform AURA 2017. A total of 159 Australian acute care hospitals (138 public

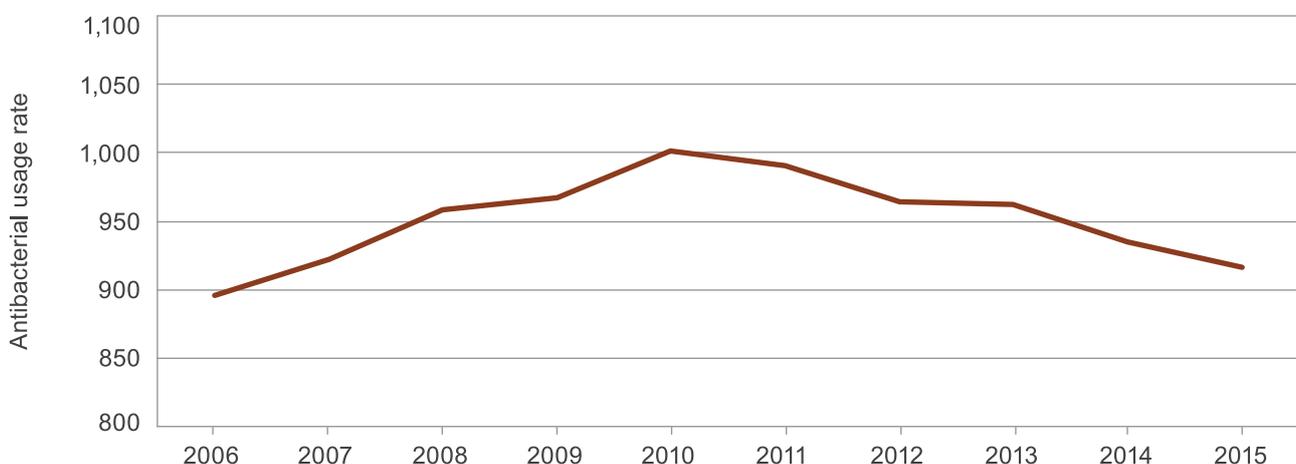
and 21 private hospitals) provided data to NAUSP in 2015, including all Principal Referral Hospitals, and more than 80% of all Public Acute Group A and Public Acute Group B Hospitals. Data on appropriateness of prescribing are from the 2015 National Antimicrobial Prescribing Survey (NAPS), which had 281 participating hospitals (213 public and 68 private) in 2015, representing 80% of Principal Referral Hospitals, 74% of Public Acute Group A Hospitals, 62% of Public Acute Group B Hospitals, and 71% of Women’s and Children’s Hospitals.

AU in Australian hospitals peaked in 2010, and has decreased gradually since then (Figure A). There has been a sustained decrease in AU in hospitals that have contributed continuously to NAUSP between 2010 and 2015.

In 2015, 20 antibacterials accounted for 93% of all antibacterials used in Australian hospitals, on the basis of defined daily doses (DDDs) per 1,000 occupied bed days (OBDs). Six antibacterials – amoxicillin-clavulanate, cefazolin, amoxicillin, flucloxacillin, doxycycline and cefalexin – represented more than half of all antibacterials used in NAUSP contributor hospitals.

Figure A: Aggregate antibacterial use in NAUSP contributor hospitals (DDD/1,000 OBD), 2006–2015

Total hospital



Source: NAUSP

The four therapeutic classes of antimicrobials most likely to drive AMR in hospitals are aminoglycosides, third- and fourth-generation cephalosporins, fluoroquinolones and macrolides. Most hospital peer groups showed a decline in the use of these four antimicrobial classes since 2011. Although there is some variation in use, rates have steadily decreased over the past five years across all states and territories.

Fluoroquinolone usage rates have continued to decrease since 2011. Most Australian hospitals and formularies have restricted the use of fluoroquinolones because they are reserved for treatment of infections that are resistant to other antimicrobials, and there are few indications for which a fluoroquinolone is the first-line treatment.

Appropriateness of prescribing in hospitals

In total, 22,021 prescriptions for 14,389 people were included in NAPS 2015. This reflects a steady increase in participation since 2013, when 12,800 prescriptions for 7,700 people were included. On the day of the Hospital NAPS survey in 2015, 40.5% of people in hospital received at least one antimicrobial.

Findings regarding appropriateness of prescribing in hospitals show improvement over the past two years. However, it is unclear whether this is because of changes in the characteristics of participating hospitals or real improvement across all hospitals. The ANCU will continue to work with a range of partners and stakeholders to promote improved prescribing practices for surgical prophylaxis.

The most common reasons prescriptions were generally deemed to be inappropriate in the 2015 NAPS were similar to those reported in AURA 2016 – an antimicrobial was not needed; the antimicrobial chosen was incorrect (spectrum too broad); or the duration, dose or frequency of treatment was incorrect.

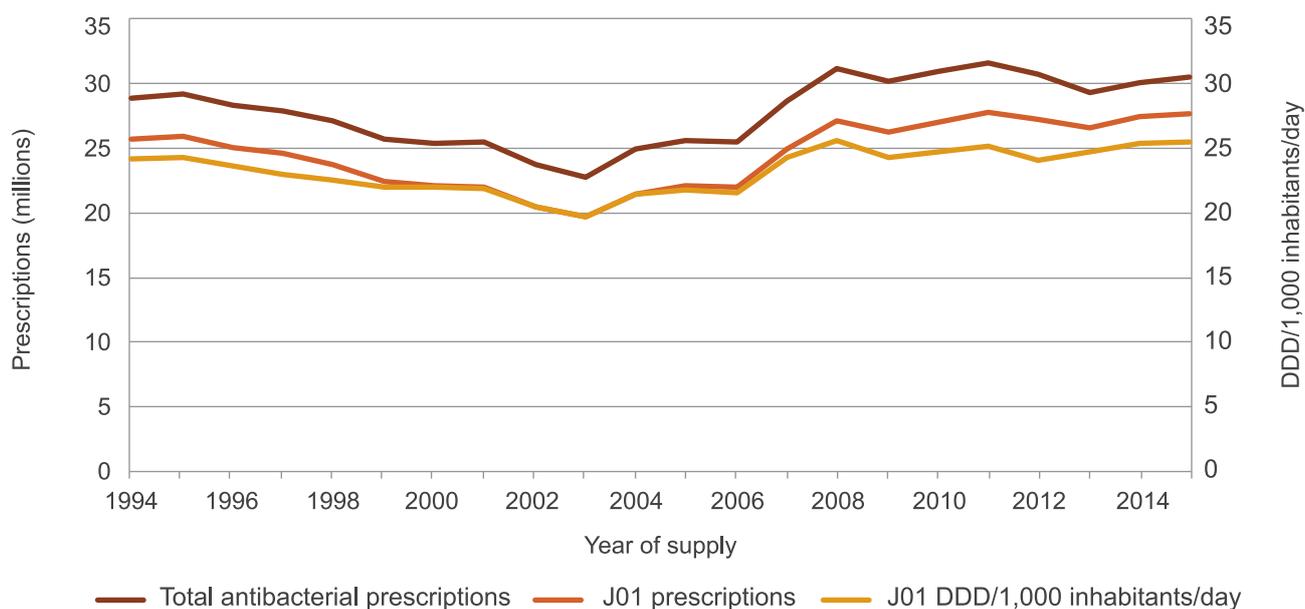
Understanding variation in prescribing rates and appropriateness of prescribing is critical to improving the quality of AU. However, there remain insufficient data to identify the factors that are driving variation in volumes and patterns of AU in Australian hospitals. Monitoring AU and appropriateness of prescribing through AURA will allow trends to be analysed to inform response strategies. The ANCU continues to work with stakeholders to improve understanding of this variation, and review opportunities to improve practice and patient care.

Antimicrobial use in the community – primary care

Most AU in Australia occurs in the community setting, which includes general practice, specialist outpatients, dental clinics and aged care homes. In 2015, around half of the Australian population (44.7%, about 10.7 million people) had at least one antimicrobial dispensed under the PBS or the RPBS. Of these, 18.5% had one antimicrobial dispensed, and 3.2% had more than six antimicrobial prescriptions dispensed, including repeats. These figures are very similar to the 2014 data reported in AURA 2016.

Around 30.5 million prescriptions for antimicrobials were dispensed under the PBS/RPBS in 2015 (around 27.7 million prescriptions for systemic antimicrobials and 2.8 million for topical antimicrobials). This represents a small increase compared with 2014.

The supply of PBS/RPBS systemic antimicrobials in 2015 totalled 27,667,198 prescriptions – a 6.7% increase in DDDs per 1,000 inhabitants per day compared with 2014. A further 2,785,173 prescriptions were supplied for non-systemic (topical) preparations, making a total of 30,452,371 prescriptions (1,280 prescriptions per 1,000 inhabitants) for antimicrobials (Figure B).

Figure B: Number of antimicrobials dispensed under the PBS/RPBS, 1994–2015**Notes:**

1. J01 is the Anatomical Therapeutic Chemical code for antibacterials for systemic use.
 2. Data relating to the number of prescriptions dispensed before April 2012 include estimates for under co-payment and private dispensing. Data relating to the number of prescriptions dispensed after April 2012 include actual under co-payment data, but no estimate for private dispensing. The data on DDD/1,000 inhabitants/day exclude some items for which there is no defined daily dose.
- Source: Drug Utilisation Sub Committee database, 2017

The 11 most commonly dispensed antimicrobials under the PBS/RPBS, by number of prescriptions, accounted for 84% of all antimicrobials dispensed in the community. Amoxicillin, cefalexin and amoxicillin-clavulanate were again the most commonly prescribed, accounting for 64.5% of prescriptions.

As for 2014, antimicrobials were most commonly dispensed in 2015 for very young people and older people. In 2015, 51% of those aged 0–4 years, 60% of those aged 65 years or over, and 76% of those aged 85 years or over were supplied at least one antimicrobial. These proportions have been generally consistent for several years, although the proportion of prescriptions dispensed for the 0–4-year age group in 2015 (51%) was lower than that reported in 2014 (57%). AU in all age groups is higher during the winter months.

Appropriateness of prescribing in the community – primary care

The Commission works with NPS MedicineWise to analyse data on patterns of systemic AU in primary care from the MedicineInsight program. MedicineInsight also provides demographic characteristics and risk factors for patients prescribed systemic antimicrobials, and assesses the appropriateness of prescribing for specific conditions such as upper respiratory tract infections and urinary tract infections.

Between 1 January and 31 December 2015, 30% of MedicineInsight patients (just under 1 million people) were prescribed systemic antimicrobials. Females and older people were more likely to receive a prescription. New South Wales had higher prescribing rates (31.1 prescriptions per 100 patients) than other states (24.5–31.0 prescriptions per 100 patients), and people living in major cities had higher rates of prescription of systemic antimicrobials than residents of other regions.

Only 23.5% of MedicineInsight patients prescribed antimicrobials in 2015 had an indication recorded for the prescription in their health record. A large proportion of patients with specifically documented types of upper respiratory tract infections (such as acute undifferentiated upper respiratory tract infection, acute tonsillitis, acute sinusitis, acute otitis media or acute bronchitis) were reported to have been prescribed an antimicrobial, despite guidelines recommending that antimicrobials are not indicated as routine therapy for these conditions. A large proportion of the antimicrobials prescribed were not consistent with the first recommendation in Australian guidelines, and concordance with guidelines varied from 27% for sinusitis to 67% for pneumonia.

The high prescribing rates for amoxicillin, amoxicillin-clavulanate and roxithromycin for upper respiratory tract infections reported by MedicineInsight accord with the data published in the annual *Report on Government Services*.

Antimicrobial resistance: key findings

Antimicrobial-resistant bacteria and their resistance genes can spread readily between people in the community, primary care services, hospitals and aged care homes, and affect the community, patients, health services and the health system. The capability of the AURA Surveillance System to identify critical antimicrobial resistances and monitor resistance will enable patterns in resistance to be more readily identified and acted on.

The priority organisms reported on in AURA 2017 are considered to be either common pathogens or of high public health importance, and where the effect of resistance is substantial in both community and hospital settings. Chapter 4 of AURA 2017 provides details of resistance in these organisms, commentary on related outcome measures and an assessment of trends, where

sufficient data are available. The Commission will continue to direct, coordinate and report on surveillance of these organisms. The list of priority organisms will undergo regular review to ensure currency for surveillance efforts; the review in 2016 did not recommend any changes to the list.

Table A provides a summary of antimicrobial resistance for the priority organisms.

Resistance trends of concern

Despite the major expansion in national data coverage, there have been few changes in resistance rates compared with 2014. Noticeable increases were seen in rates of fluoroquinolone resistance in *Escherichia coli* and *Shigella sonnei*, and in rates of reduced susceptibility and resistance to benzylpenicillin in *Neisseria meningitidis*. Rates of resistance in the community remain relatively stable compared with 2014, and are low by world standards.

Critical antimicrobial resistances: key findings

The establishment of CARAlert was the most significant new development for AURA in 2016. CARAlert provides timely national data on organisms that are considered to be important to human health and that are resistant to last-line antimicrobial agents.

Of the 673 results submitted to CARAlert in 2016, 48% were carbapenemase-producing Enterobacteriaceae. The IMP-type carbapenemase is now endemic on the Australian eastern seaboard in multiple species of Enterobacteriaceae, particularly *Enterobacter cloacae*. There is no evidence that other carbapenemases have become established in Australia.

No reports of *Streptococcus pyogenes* with reduced susceptibility to penicillin were submitted to the system in 2016.

Table A: Summary of antimicrobial resistance for high-priority organisms

Organism	Main types of infection	Where seen	Important antimicrobials for treatment	% resistant, 2014	% resistant, 2015
<i>Acinetobacter baumannii</i>	Ventilator-associated pneumonia, severe burn infections	Intensive care units, burn units	Ciprofloxacin	4.1	3.1
			Gentamicin	2.4	1.6
			Meropenem	3.6	2.6
<i>Escherichia coli</i>	Urinary tract infections, biliary tract infections, other intra-abdominal infections, septicaemia	Community, hospitals	Amoxicillin-clavulanate	18.2-21.1	9.4-20.1
			Ampicillin/amoxicillin	42.3-51.3	42.9-53.2
			Cefazolin	15.2-25.0	15.8-24.8
			Ceftriaxone	5.1-12.4	6.4-10.8
			Ciprofloxacin	6.2-8.7	7.3-11.2
			Gentamicin	4.5-7.0	4.9-7.5
			Piperacillin-tazobactam	5.3-9.4	4.6-7.3
			Trimethoprim	21.0-29.4	21.8-31.3
			Multidrug resistant	13.1	23.7
<i>Enterobacter cloacae</i>	Urinary tract infections, other intra-abdominal infections, septicaemia	Hospitals	Ceftriaxone	23.8-28.5	22.8-36.2
			Piperacillin-tazobactam	24.3-32.2	19.5-26.6
			Trimethoprim	18.3-21.3	10.9-20.4
			Gentamicin	7.2-7.8	5.4-9.2
			Ciprofloxacin	3.7-5.2	3.1-6.2
			Meropenem	1.1-2.6	1.4-2.2
<i>Enterococcus faecalis</i>	Urinary tract infections, biliary tract infections, other intra-abdominal infections, septicaemia, endocarditis (heart valve infections)	Community, hospitals	Ampicillin	0.3-0.6	0.1-0.5
			Vancomycin	0.3-0.4	0.1-0.3
<i>Enterococcus faecium</i>	Urinary tract infections, biliary tract infections, other intra-abdominal infections, septicaemia	Hospitals	Ampicillin	83.3-94.5	86.3-95.9
			Linezolid	0.2-1.1	0.0-0.4
			Vancomycin	45.7-49.9	48.7-56.8

continued

Table A: continued

Organism	Main types of infection	Where seen	Important antimicrobials for treatment	% resistant, 2014	% resistant, 2015
<i>Klebsiella pneumoniae</i>	Urinary tract infections, other intra-abdominal infections, septicaemia	Community	Amoxicillin-clavulanate	6.2-9.4	4.4-7.3
			Cefazolin	6.6-10.6	6.8-10.8
			Ceftriaxone	4.3-6.6	5.0-7.0
			Ciprofloxacin	4.5-6.2	3.7-4.8
			Gentamicin	3.1-4.9	3.2-4.2
			Piperacillin-tazobactam	7.6-8.9	6.0-7.7
			Trimethoprim	12.3-16.6	10.1-14.1
			Multidrug resistant	9.0	10.2
<i>Mycobacterium tuberculosis</i>	Pulmonary tuberculosis, extrapulmonary tuberculosis	Community	Ethambutol	1.2	0.9
			Isoniazid	8.5	10.7
			Pyrazinamide	2.1	2.7
			Rifampicin	2.4	3.8
			Multidrug resistant	1.7	1.9
<i>Neisseria gonorrhoeae</i>	Gonorrhoea	Community	Azithromycin	2.5	2.6
			Benzylpenicillin	28.5	22.5
			Ceftriaxone (decreased susceptibility)	5.4	1.8
			Ciprofloxacin	36.4	27.2
<i>Neisseria meningitidis</i>	Septicaemia	Community	Benzylpenicillin (decreased susceptibility)	15.8	25.6
			Ceftriaxone	0.0	0.0
			Ciprofloxacin	0.0	0.0
			Rifampicin	2.1	0.9
<i>Pseudomonas aeruginosa</i>	Urinary tract infections, burn infections, cystic fibrosis exacerbations	Community, hospitals	Ceftazidime	4.5	4.5
			Ciprofloxacin	6.7	6.2
			Gentamicin	5.3	5.2
			Meropenem	4.0	3.5
			Piperacillin-tazobactam	10.3	7.3
<i>Salmonella</i> species (non-typhoidal)	Gastroenteritis, septicaemia	Community	Ampicillin	6.7-7.7	1.6-7.1
			Ceftriaxone	0.6-1.9	0.0-1.5
			Ciprofloxacin	0.0-1.1	0.0-2.2
<i>Salmonella</i> Typhi/Paratyphi	Typhoid fever (septicaemia)	Community	Ampicillin	2.3	4.9
			Ceftriaxone	0.0	1.2
			Ciprofloxacin	12.2	51.4

continued

Table A: continued

Organism	Main types of infection	Where seen	Important antimicrobials for treatment	% resistant, 2014	% resistant, 2015
<i>Shigella flexneri</i>	Bacillary dysentery	Community	Ampicillin	57.1	70.0
			Ceftriaxone	0.0	0.0
			Ciprofloxacin	0.0	0.0
<i>Shigella sonnei</i>	Bacillary dysentery	Community	Ampicillin	10.6	18.2
			Ceftriaxone	3.1	6.8
			Ciprofloxacin	9.4	20.3
<i>Staphylococcus aureus</i>	Skin, wound and soft tissue infections; bone and joint infections; device-related infections; septicaemia; endocarditis (heart valve infections)	Community, hospitals	Benzylpenicillin	83.1–88.7	83.2–87.7
			Clindamycin	7.1–10.0	8.1–14.6
			Erythromycin (and other macrolides)	16.5–17.0	14.4–17.0
			Oxacillin (methicillin)	15.8–17.4	11.8–15.0
<i>Staphylococcus aureus</i> (methicillin resistant)	Skin, wound and soft tissue infections; bone and joint infections; device-related infections; septicaemia; endocarditis (heart valve infections)	Community, hospitals	Clindamycin	14.2–19.6	22.9–23.7
			Fusidic acid	4.6–5.9	4.4–5.2
			Linezolid	0.1–0.3	0.0–0.1
			Rifampicin	0.8–0.9	0.8–1.9
			Trimethoprim-sulfamethoxazole	2.5–11.9	7.0–11.7
			Vancomycin	0.0	0.0
<i>Streptococcus agalactiae</i>	Skin and soft tissue infections, urinary tract infections, newborn septicaemia	Community	Benzylpenicillin	0.0	0.0
			Clindamycin	17.1	22.4
			Erythromycin (and other macrolides)	22.7	26.7
			Trimethoprim	17.2	13.9
<i>Streptococcus pneumoniae</i>	Otitis media (middle ear infections), sinusitis, acute exacerbation of chronic obstructive pulmonary disease, pneumonia, meningitis, septicaemia	Community	Benzylpenicillin (outside the central nervous system)	2.0–2.3	2.8–4.6
			Erythromycin (and other macrolides)	21.1–25.9	14.5–24.1
			Tetracycline (and doxycycline)	21.1–25.6	15.1–24.4
<i>Streptococcus pyogenes</i>	Skin, wound and soft tissue infections; septicaemia	Community	Benzylpenicillin	0.0	0.0
			Erythromycin (and other macrolides)	3.4	4.1
			Clindamycin	-	12.3

- = not reported (either not tested or tested against an inadequate number of isolates)

Azithromycin-nonsusceptible *Neisseria gonorrhoeae* is more common in Australia than originally thought, and seems to be spreading and appearing in different states at different times.

The number of records in the database to date is too small to allow specific conclusions to be drawn. However, the data undergo regular epidemiological analysis, and as the number of reports increases to enable meaningful analyses of trends and their implications, these aspects will also be reported on.

Chapter 5 of AURA 2017 includes a complete description of the data from the first calendar year of operation of CARAlert.

Focus areas: key findings

Chapter 6 of AURA 2017 provides commentary on a number of areas of focus for AURA that highlight the importance of surveillance and the responses that may be required. It also includes comparisons of Australia's AU and AMR with other countries.

Two areas of focus include the emerging healthcare issue of VRE, which increases pressure on the only two or three reserved antimicrobials that can be used to treat serious infections, and the Queensland clone of MRSA, which has become the dominant community-associated MRSA clone in Australia.

Three susceptibility testing systems are currently used in laboratories in Australia: Clinical and Laboratory Standards Institute, European Committee on Antimicrobial Susceptibility Testing, and Calibrated Dichotomous Sensitivity (developed in Australia). The AURA Surveillance System analyses and reports on data longitudinally, and use of different testing systems can make it difficult to compare resistance rates. A nationally standardised approach would simplify data collection and

analysis, assist in benchmarking and increase confidence in long-term trends.

Rates of resistance in Australia compared with other countries have changed little between 2014 and 2015. Antimicrobial dispensing rates in the Australian community are substantially higher than in benchmark countries. Rates of resistance to fluoroquinolones and third-generation cephalosporins in *Escherichia coli* and *Klebsiella pneumoniae* remain low in Australia compared with most European countries, although they are now increasing. However, compared with European countries, Australia ranks towards the middle in rates of resistance to methicillin in *Staphylococcus aureus*, and higher than any European country in rates of resistance to vancomycin in *Enterococcus faecium*.

Future developments

The range of reports now available through the AURA Surveillance System supports clinicians, health service managers, policy makers and program developers, and will continue to strengthen strategies to prevent and contain AMR and improve antimicrobial prescribing. These reports demonstrate that an effective surveillance system can greatly improve understanding of how antimicrobials are used in Australia, and increase our knowledge of the priority organisms that are resistant to antimicrobials.

Over time, progressive AURA publications will allow trends to be monitored and reported, and more specific action to be taken. The Commission's ANCU will continue to work with key stakeholders to focus on the analyses and reports that will be of greatest benefit in responding to the gaps identified. This will better inform action at the local, regional, state and territory, and national levels to prevent and contain the spread of AMR.

The ANCU will use the resources available to increase data volume and representativeness, and improve data analysis and interpretation. Data definitions and collection methods will be more closely reviewed to improve the validity and consistency of approach across the AURA program elements. This will be a focus of work to improve benchmarking and comparability across hospitals and internationally. The Commission will continue to monitor emerging resistances and changes in patterns of resistance, and ensure that they can be rapidly identified and communicated to the states and territories to contain and prevent outbreaks.

Other areas under consideration by the ANCU for further investigation or action include:

- Assessing factors that drive variation in AU and prescribing across jurisdictions
- Improving appropriateness of prescribing in hospitals (particularly for surgical prophylaxis) and the community (particularly for upper respiratory tract infections)
- Conducting more detailed analyses of CARAlert data and reporting this to the states and territories.

AURA 2017 demonstrates the effect of the Commission's actions to improving the diversity and utility of surveillance data, and has embedded mechanisms to appropriately collect valuable surveillance data. The foundation for future growth and development of AMR and AU surveillance in Australia has been achieved and allows for further improvements to be made. Collaboration and cooperation across the public and private sectors in all states and territories will continue to be essential to the reliability and sustainability of the system.

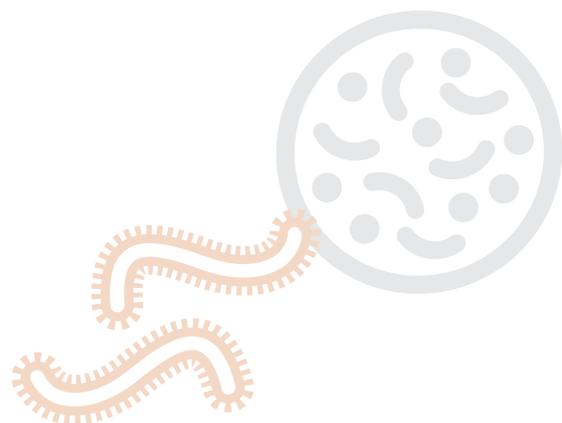


Chapter 1

Introduction

Key messages

- Antimicrobial resistance (AMR) has a direct effect on patient care and creates a set of critical ongoing challenges to health service delivery around the world.
- Comprehensive, coordinated and effective surveillance of AMR and antimicrobial use (AU) is therefore a national priority. Surveillance data can be used to develop and monitor strategies to prevent and contain AMR.
- The Antimicrobial Use and Resistance in Australia (AURA) Surveillance System was established to coordinate data collection and analyses, to provide a comprehensive and integrated picture of AU and AMR across Australia, and patterns and trends over time.
- AURA 2017 is the second report of its type on AMR and AU in Australia. It includes data about organisms that have been determined to be a priority for Australia, the volume of AU, the appropriateness of antimicrobial prescribing and key emerging issues for AMR, and a comparison of Australia's situation with other countries.



Antimicrobial resistance (AMR) is one of the most significant challenges for the provision of safe, high-quality health services across the world. This chapter provides context and background to the importance of AMR as a healthcare issue, along with information about the Australian strategic policy context and the contribution of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System in the response to AMR.

1.1 Background

Australia has adopted a One Health approach to antimicrobial resistance (AMR). This involves a coordinated, collaborative, multidisciplinary and cross-sectoral approach to the development and implementation of health strategies for people, animals and the environment. National direction on AMR is provided by the AMR Prevention and Containment Steering Group, which is led by the secretaries of the Australian Government departments of Health, and Agriculture and Water Resources, and includes the Australian Government Chief Medical Officer and Chief Veterinary Officer.

In 2013, based on the outcomes of the Australian One Health Resistance Colloquium, the Department of Health engaged the Australian Commission on Safety and Quality in Health Care (the Commission) to establish a nationally coordinated system for surveillance of AMR and antimicrobial use (AU) for human health.

About the Commission

The Commission was established in 2006 by the Australian, state and territory governments to lead and coordinate national improvements in safety and quality in health care. In 2011, the federal parliament passed the *National Health Reform Act 2011*, which established the Commission as a corporate Commonwealth entity under the *Public Governance, Performance and Accountability Act 2013*. The Commission's

governance structure is determined by these Acts, and the Commission is jointly funded by all governments on a cost-sharing basis.

The Commission has well-established processes to work in consultation with health ministers and their departments to ensure effective programs of work to improve safety and quality in healthcare delivery. This includes AMR-related initiatives focusing on infection control, antimicrobial stewardship (AMS) and medication safety programs, and reporting on AMR and AU surveillance data. The Commission also works in partnership with patients, consumers, clinicians, managers, policymakers and healthcare organisations to achieve a sustainable, safe and high-quality health system.

About the Antimicrobial Use and Resistance in Australia Surveillance System

The Commission established the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System as a national system for surveillance of AMR and AU (see Box 1.1). The strategy was to partner with existing AMR and AU surveillance programs through clear governance arrangements and contracts to enable a comprehensive picture of patterns and trends in AU and AMR. The Commission conducted wide-ranging consultation on, and review of, existing surveillance systems to identify the requirements for an effective national system. Collaborations were developed with a range of stakeholders to build and improve surveillance infrastructure, and coordinate efforts to collect, analyse and report AMR and AU data.

Where gaps in surveillance were identified, new systems were established, such as the National Alert System for Critical Antimicrobial Resistances (CARAlert). CARAlert combines the information on critical antimicrobial resistances (CARs) that is currently provided to clinicians with a system to inform program and systems

managers, which allows timely responses at the local, network, and state and territory levels.

The Commission has established a systematic approach to improve data representativeness, collection analytics and accessibility. As a result, AURA publications since 2014 have reported on improved data and information on AU and AMR in the public and private hospital, aged care and community settings across Australia. These improvements have enabled more informed strategies and programs to prevent and contain AMR. Data from AURA have been provided to clinicians, policy and program developers, health service managers and executives, state and territory governments, and the Australian Government.

In 2015, the Australian Government released Australia's first strategy on AMR, *National Antimicrobial Resistance Strategy 2015–2019*¹, which outlined the framework to address AMR using a One Health approach. The strategy aligns with the World Health Organization Global Action Plan on Antimicrobial Resistance², which was released in 2015 and endorsed at the United

Nations General Assembly high-level meeting on AMR on 21 September 2016.³ The implementation plan for the strategy was released in November 2016.⁴ The establishment of AURA has ensured that human health aspects can contribute to One Health objectives. The Commission will work with departments and other agencies involved in the agriculture, veterinary and environment sectors to promote integrated surveillance over time.

The AURA Surveillance System, and the Commission's work on the National Safety and Quality Health Service (NSQHS) Standards⁵ – particularly the Preventing and Controlling Healthcare Associated Infection Standard – support the following objectives of the strategy:

- Objective 1 – Increase awareness and understanding of AMR, its implications and actions to combat it, through effective communication, education and training
- Objective 2 – Implement effective AMS practices across human health and animal care settings to ensure the appropriate and judicious prescribing, dispensing and administering of antimicrobials

● **Box 1.1: Role of the Antimicrobial Use and Resistance in Australia Surveillance System**

The Antimicrobial Use and Resistance in Australia Surveillance System:

- Provides the strategic framework for the operation of effective surveillance and reporting of antimicrobial use (AU) and antimicrobial resistance (AMR)
- Improves quality, coverage and utility of existing high-quality data collections on AU and AMR through improved integration and coordination
- Provides more detailed analyses across data collections, including opportunities for analysing relationships between AU and AMR, at a system level
- Provides systematic, coordinated and centralised national reporting on AU and AMR
- Establishes new data collections, where needed, such as the systematic and timely identification of the emergence of critical antimicrobial resistances
- Provides a means for rapidly consulting and communicating with stakeholders to further improve the system and its reporting, and to better inform AMR prevention and control strategies.

- Objective 3 – Develop nationally coordinated One Health surveillance of AMR and AU
- Objective 4 – Improve infection prevention and control measures across human health and animal care settings to help prevent infections and the spread of resistance.

The first report on data from the AURA Surveillance System was published in June 2016.⁶ The patterns and trends identified in AURA reports guide improvements in infection control, AMS and antimicrobial prescribing practices.

Antimicrobial Use and Resistance in Australia program partners and data sources

Four core long-term surveillance programs provide the foundation for the AURA Surveillance System:

- Australian Group on Antimicrobial Resistance
- National Antimicrobial Prescribing Survey
- National Antimicrobial Utilisation Surveillance Program
- Queensland Health OrgTRx System, which is the base for the National Passive AMR Surveillance System.

In addition, data and reports are gathered from:

- The National Neisseria Network, on *Neisseria gonorrhoeae* and *N. meningitidis*
- The National Notifiable Diseases Surveillance System, on *Mycobacterium tuberculosis*
- The Pharmaceutical Benefits Scheme (PBS) and the Repatriation Pharmaceutical Benefits Scheme (RPBS)
- The NPS MedicineWise MedicineInsight program
- Sullivan Nicolaides Pathology, on rates of AMR from the community and private hospital settings.

During 2016, the Commission also established CARAlert to collect surveillance data on priority organisms with resistance to last-

line antimicrobials (see Chapter 5 for more information about CARAlert).

Each of the partner programs provides valuable data on AU and AMR that cover selected organisms or antimicrobials from the community and hospitals. The programs use a range of methods, sampling techniques and sources, and have largely been set up to provide data at the local or state and territory levels for specific purposes.

The coverage, capture and content of these data have varied. However, each of these programs is now operating within the framework of AURA to provide an integrated and coordinated picture of AU and AMR in Australia, and this system will continue to improve.

Important functions of AURA include coordinating data from across the public and private hospital, aged care and primary care settings, and engaging with providers to help them use the AURA data and reports to improve clinical practice, and prevent and contain AMR.

1.2 Australian healthcare system context

The Australian healthcare system is multifaceted. Services are provided in both the public and private sectors, in institutional and community settings. Healthcare providers include individual clinicians (such as doctors, nurses and allied health professionals), and organisational entities such as hospitals, primary care services, and government and non-government agencies. A comprehensive and complex range of services is provided across Australia, including primary health services; emergency and acute admitted and non-admitted health services in hospitals, day-stay facilities and home-based care; admitted and non-admitted subacute and non-acute services such as rehabilitation and palliative care; and community-based services, such as pharmacies.

Medicare is the Australian Government-funded health insurance scheme that provides access to free or subsidised healthcare services to the Australian population. It provides free hospital services for public patients in public hospitals, subsidises private patients for hospital services, and provides benefits for out-of-hospital medical services such as consultations with general practitioners or specialists.

The Australian Government's PBS and RPBS provide subsidised access to a wide range of medicines for all Australians. Under the PBS/RPBS, patient contributions towards medication costs at pharmacies are capped, and there is a Safety Net Scheme to protect people with high medication needs.

The most recently available analyses from the Australian Institute of Health and Welfare show that around 69% of total expenditure on health in 2013–14 was funded by governments.⁷ The Australian Government contributed approximately 42%, and state and territory governments 27%. The remainder included contributions by patients (17%), private health insurers (8%) and accident compensation schemes (5%).⁸

Public hospitals are funded by the Australian, and state and territory governments, and managed by the state and territory governments. In 2013–14, public hospitals provided about 67% of all acute admitted care. During the previous decade, growth in hospitalisations was higher in private hospitals than in public hospitals.⁸

The majority of services provided by doctors (general practitioners and specialists) occurs in the private sector. General practitioners and pharmacists are largely self-employed, and are funded through a combination of government subsidies such as Medicare and the Practice Incentive Program, and out-of-pocket payments from patients. In 2014–15, total recurrent Australian Government expenditure on general practice was \$8.3 billion, and total expenditure

on the PBS and RPBS for prescription medicines filled at pharmacies was around \$7.4 billion.⁹

The private sector also includes large diagnostic services. Ownership of private hospitals is primarily limited to large for-profit and not-for-profit organisations.

Australian governments and health service organisations are committed to improving the safety and quality of health care, and the Commission is central to this process. The NSQHS Standards were developed by the Commission in collaboration with states and territories, clinical experts, patients and carers. The primary aims of the NSQHS Standards are to protect the public from harm and to improve the quality of health service provision. They provide a quality-assurance mechanism that tests whether relevant systems are in place to ensure that expected standards of safety and quality are met.

There are 10 NSQHS Standards, which cover high-prevalence adverse events, healthcare-associated infections, medication safety, patient identification and procedure matching, clinical handover, the prevention and management of pressure injuries, the prevention of falls, and responding to clinical deterioration. Importantly, these NSQHS Standards have provided, for the first time, a nationally consistent statement about the standard of care that consumers can expect from their health service organisations.

The Preventing and Controlling Healthcare Associated Infection Standard requires health service organisations to monitor patterns of AU, and use this information to guide AMS practices and meet infection control requirements.¹⁰ Data from the AURA Surveillance System directly support this standard.

1.3 Importance of antimicrobial resistance

AMR occurs when a microorganism develops resistance to an antimicrobial that was previously an effective treatment. As a result, infections caused by the resistant organism may need to be treated with other antimicrobials, which can have more severe side effects, be more expensive or take longer to work. In some severe cases, resistant organisms may not be able to be treated by any currently available antimicrobials.

Antimicrobial resistance contributes to patient illness and death. It increases the complexity of treatment and the duration of hospital stay, and places a significant burden on patients, health service organisations and the health system.^{11,12}

International evidence consistently demonstrates the growing effect that AMR is having on human health, and studies confirm that increasing numbers of infections in health service organisations and in the community are caused by resistant pathogens.¹³ A significant contributor to increasing AMR is the inappropriate use of antimicrobials.

Slowing the rate of increase in resistance, preparing for and responding to new and emerging threats, and ensuring that antimicrobials are used appropriately are all components of the work undertaken by the Commission to ensure the safety and quality of health care in Australia.

A review by the London School of Hygiene and Tropical Medicine in the United Kingdom (UK) estimated the economic burden of AMR, finding that it led to additional costs that ranged from £5 to more than £20,000 per episode of care in hospital (equivalent to A\$10 to more than

A\$41,200). The authors proposed that these estimates are modest, because they are largely based on the incremental costs of treating resistant infections compared with susceptible infections.¹⁴

Most studies focus on additional healthcare costs, morbidity and mortality in individual patients with a subset of resistant organisms, and tend not to consider the broader costs to society and the healthcare system.¹⁴⁻¹⁶ The broader implications and costs include those borne by the community as a result of the reduced effectiveness of antimicrobials over time. These may include reduced productivity through extended illness, and the potential loss of patients' ability to safely undergo advanced surgical procedures and treatments, such as chemotherapy, in the future.

AMR has significant and direct effects on patient care. For example, people currently undergoing hip replacements receive standard prophylactic antimicrobials and experience infection rates of around 0.5–2.0%.¹⁴ If access to effective antimicrobials were reduced, postoperative infection rates may rise to around 40–50%, and up to 30% of these patients could die from these infections.¹⁴

Beyond the impact of reduced effectiveness of antimicrobials, there can also be substantial costs associated with failing to identify and manage outbreaks of resistant organisms in a timely way. In 1995, the cost of containing an outbreak of methicillin-resistant *Staphylococcus aureus* in a district general hospital in the UK was estimated to be more than £400,000 (A\$824,000).¹⁷ If this type of outbreak becomes more frequent, the cost to organisations and health systems could continue to escalate.

A 2014 UK review on AMR investigated the global economic cost of antimicrobial-resistant infections. The results suggested that, if the current trend of increasing AMR continues, by 2050 around 10 million people may die every year as a direct result of AMR. Gross

domestic product (GDP) would decrease by 2.0–3.5% as a result of AMR, which would cost the world's economies around US\$100 trillion (A\$140 trillion).¹⁶ This is likely to be an underestimate of the real costs of AMR, because the review focused on the impact on GDP, and did not consider social and health costs.

Regardless of the dollar amount, there is broad consensus that AMR-related costs to, and effects on, patients, health service organisations and health systems are likely to be significant in the short to medium term because of longer treatment and recovery times, increased use of medicines, and increased risk of complications. In addition, as indicated in many reports, if antimicrobials become ineffective, a range of important treatments and healthcare services (such as surgery and chemotherapy for cancer) may no longer be a viable option, which would have a negative effect on the nature of service delivery and the effectiveness of the healthcare system in the long term.¹⁴ It is for these reasons that AMR is considered a significant threat to human health.

● **Box 1.2: What does surveillance do?**

Surveillance of antimicrobial use (AU) and antimicrobial resistance (AMR):

- Measures the size, burden, relative importance and, where possible, effects of AMR
- Measures the level of exposure (use) and the appropriateness of AU
- Detects critical AMRs early to ensure that effective action can be taken
- Enables changes in AMR and AU to be monitored
- Provides information on the effectiveness of measures to control AU and contain AMR.

1.4 Importance of surveillance

Comprehensive and coordinated surveillance is a critical requirement of efforts to control AMR (Box 1.2).¹² The information generated through AURA informs and supports strategies to prevent and contain AMR. Successive international and Australian reports on AMR have identified the effective coordination of national surveillance as a foundation for reducing the adverse effects of AMR, and the Commission's efforts in the establishment of AURA have led to improved integration and reporting of surveillance data.

Use of surveillance data can result in earlier detection of, and response to, CARs, and has the potential to reduce overall population impact in an outbreak. Broader health system benefits can also be gained through reduced length of stay and overall improvements in bed capacity.

At the local level, organisations and clinicians can use surveillance data to develop guidance and protocols that maximise the appropriate, effective and efficient use of antimicrobials.

More timely access to relevant data on AMR and AU will more effectively inform policy decisions, such as development or revision of antimicrobial prescribing guidelines, and help identify priorities for public health action, such as education campaigns or regulatory measures.

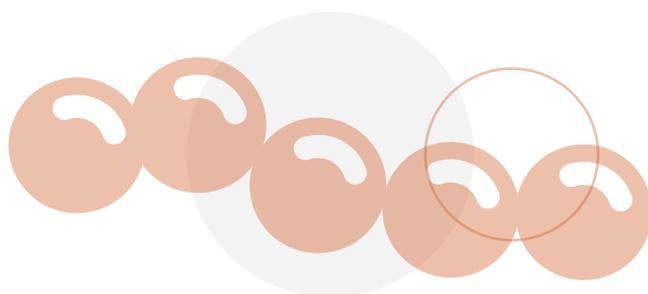
Table 1.1 provides some examples of how surveillance data for AU and AMR can be used, and the expected outcomes.

A lack of surveillance, or poor or ineffective reporting, can lead to misdirected and inefficient policies and programs, along with poor use of resources through inappropriate or inefficient therapies. Importantly, these deficits can also lead to increased morbidity and mortality if patients are given ineffective or inappropriate medicines.¹⁸

Table 1.1: Uses and outcomes of national surveillance of antimicrobial use and resistance at different health system levels

Level	Use of surveillance data	Effect or outcome
Global	Inform strategies to prevent and contain AMR, including the response to the Global Action Plan on Antimicrobial Resistance	Coordinated efforts internationally Avoidance of duplication of effort and inefficient use of resources Improved opportunities to reduce global spread
National	Inform policy and program development Promote more efficient and effective use of resources Inform the need to develop and revise guidelines Inform public health priorities Inform regulatory decisions Coordinate, where necessary, a system-wide response to CARs	Coordinated and integrated efforts across Australia Increased awareness of AMR and the One Health approach
State and territory	Inform policy and program development Promote more efficient and effective use of resources Inform the need to develop and revise guidelines Inform public health priorities Inform regulatory decisions Detect and respond to CARs and outbreaks in a more timely and systematic way	Improved knowledge of local AMR profiles Timely response to emerging resistance Appropriate and effective use of antimicrobials
Healthcare services	Inform clinical practice Inform policy development Develop local strategies to improve antimicrobial stewardship Detect and respond to outbreaks of resistant organisms	Appropriate and effective use of antimicrobials Improved capacity for timely response to emerging AMR
Individual	Raise awareness of appropriate antimicrobial use in the community	Appropriate use of antimicrobials as prescribed Decreased complications from unnecessary or inappropriate antimicrobial therapy

AMR = antimicrobial resistance; CAR = critical antimicrobial resistance



Reporting the information gained from an effective surveillance program to policymakers and clinicians will have positive effects at all levels of the health system. At a policy level, programs will be better targeted at the areas of greatest need, improving their effect and efficiency. At a patient care level, information

that is robust and accessible may be able to contribute to more effective prescribing, creating the potential for better health outcomes, and reducing healthcare costs (also see Box 1.3).¹⁸

● **Box 1.3: Antimicrobial stewardship**

Antimicrobial stewardship (AMS) involves a multidisciplinary approach to implementing strategies to improve the appropriate and safe use of antimicrobials by health service organisations.¹⁹

Effective AMS strategies are comprehensive in approach and incorporate the AMS Clinical Care Standard. Key strategies include:

- Educating and assessing the competence of prescribers
- Reviewing antimicrobial prescribing and providing feedback to clinicians regarding their prescribing practices
- Establishing an antimicrobial formulary that includes restriction rules and approval processes
- Ensuring that clinicians have ready access to current, evidence-based Australian therapeutic guidelines
- Developing point-of-care interventions to improve appropriate prescribing
- Measuring the performance of AMS programs

- Ensuring that the clinical microbiology laboratory uses selective reporting of susceptibility testing results, consistent with the organisation's antimicrobial treatment guidelines.

AMS is a core criterion under the Preventing and Controlling Healthcare Associated Infection Standard (Standard 3) of the National Safety and Quality Health Service Standards. AMS is critical to improving patient outcomes, reducing adverse effects relating to antimicrobial treatment and containing the spread of antimicrobial resistance. Implementing an AMS program requires an understanding of the rates of antimicrobial prescribing within the service. Programs in Australia – such as the National Antimicrobial Prescribing Survey, and the National Antimicrobial Utilisation and Surveillance Program – can provide these types of data. The Antimicrobial Use and Resistance in Australia project will offer further opportunities to report across these programs.

1.5 AURA 2017 report

AURA 2017 is the second national AURA report. It builds on the first national report from 2016 by providing a more comprehensive picture of AU and AMR rates, patterns and trends, using a greater breadth and volume of surveillance data. In addition, data and analyses from the new CARAlert system provide a national picture of CARs across the health and aged care settings, which has not previously been available. This information will also support the development of actions to implement the National Antimicrobial Resistance Strategy.

AURA 2017 provides further detail about the key AMR issues for Australia, with a broader range of data on the most frequently used antimicrobials and a designated group of priority organisms. Where available, the report includes data and analyses on patterns and trends:

- For antimicrobial prescribing and dispensing in hospitals and the community
- For the appropriateness of antimicrobial prescribing
- For resistance in priority organisms to key antimicrobials in acute care, aged care homes and the community
- To provide evidence to inform state and territory AMR prevention and containment strategies.

AURA 2017 highlights some issues for AU and AMR in Australia, and reflects on some comparisons with other countries that were reviewed in AURA 2016.

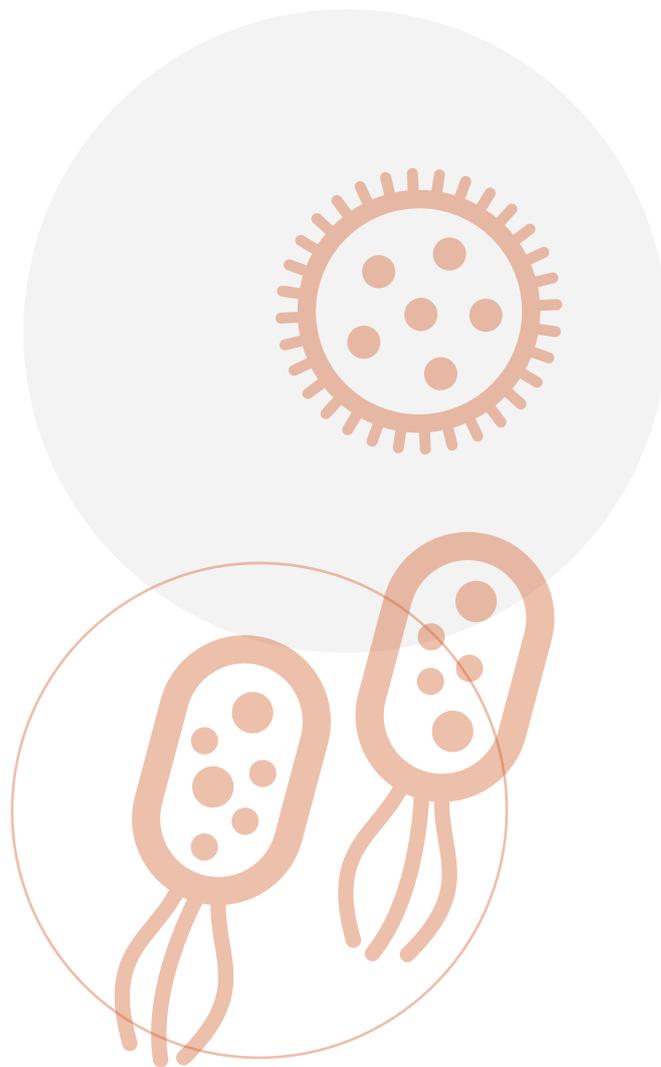
AURA 2017 includes data on the appropriateness of AU, which is a feature of Australian surveillance that is not yet produced in overseas surveillance reports.

The Commission continues to expand the range of surveillance to cover all elements of the AURA framework (see Figure 2.1 in Chapter 2), and provide an increasingly comprehensive understanding of AU and AMR in Australia.

This report integrates data from across the partner programs and organisations, and includes participation from all states and territories, and the private sector. Details on the data sources and the methods for individual collections are included in Chapter 2 and Appendix 1.

The Commission continues to engage new participants and partners to strengthen the integrity and utility of the AURA Surveillance System. The coordination unit will work with each of the partner programs, the states and territories, the Australian Government, the private sector, and clinicians to ensure that participation continues to grow, and that data are increasingly consistent and comparable. Data will also be analysed from medical, scientific and epidemiology perspectives to inform response strategies. The Commission's governance arrangements, clinician networks, and relationships with consumers and governments will enable information to be reported in formats that will be most useful to these diverse audiences.

The Commission thanks each of the organisations and networks that contribute to the report and to the AURA Surveillance System, and encourages greater participation and use of the surveillance data by all those involved in health service delivery.



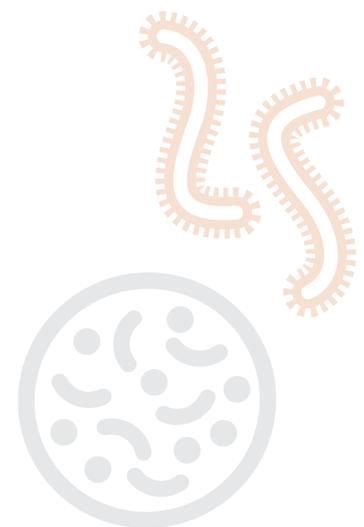


Chapter 2

Data sources and methods

Key messages

- The Antimicrobial Use and Resistance in Australia (AURA) Surveillance System was established by the Australian Commission on Safety and Quality in Health Care as a comprehensive approach to surveillance of both antimicrobial use (AU) and antimicrobial resistance (AMR) in hospitals and in the community, from passive and targeted systems.
- Data on AU and its appropriateness are sourced from the National Antimicrobial Prescribing Survey, the National Antimicrobial Utilisation Surveillance Program, the NPS MedicineWise MedicineInsight program and the Pharmaceutical Benefits Scheme/Repatriation Pharmaceutical Benefits Scheme.
- Data on AMR are sourced from the Australian Group on Antimicrobial Resistance, the National Passive AMR Surveillance System (based on the Queensland Health OrgTRx system), the National Neisseria Network, the National Notifiable Diseases Surveillance System, Sullivan Nicolaides Pathology and the National Alert System for Critical Antimicrobial Resistances (CARAlert).



The AURA National Coordination Unit (ANCU) of the Australian Commission on Safety and Quality in Health Care (the Commission) has been working with multiple organisations and programs to specify the data and information required from them, to coordinate all elements of the national system. The overall strategy is supported by a detailed picture of each data source, and methods and purposes of the data collections, and an understanding of any limitations when using the data. Effective coordination, efficient analysis and accurate reporting by the Commission will inform strategies for local, state and territory, and national health systems over time. They will also help identify opportunities to improve the system, and to improve AMR control and prevention.

This chapter describes the types and sources of data used in the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System.

2.1 Types of data and information collected under the Antimicrobial Use and Resistance in Australia Surveillance System

The framework of the component parts of the AURA Surveillance System, and their data sources, is shown in Figure 2.1. The framework encompasses data from the community and acute health sectors. This report includes data predominantly from 2015. It also includes additional data from 2016 from the newest element of AURA, which provides surveillance of critical antimicrobial resistances. The National Alert System for Critical Antimicrobial Resistances (CARAlert) was highlighted as a new development in the AURA 2016 report, and was established in March 2016. Further detail is provided in Chapter 5.

The partnership approach of AURA, which uses a combination of passive and targeted surveillance, is necessary to achieve comprehensive and effective surveillance, and to support timely and appropriate response strategies.

Passive surveillance is the use of data that are already collected for other purposes, to identify patterns and trends in antimicrobial resistance (AMR) and antimicrobial use (AU).

Targeted surveillance is where the primary purpose of collecting data is to identify trends and patterns in AMR and AU.

Passive surveillance is the use of data that are already collected for other purposes, to identify patterns and trends in AMR and AU. Targeted surveillance is where the primary purpose of collecting data is to identify trends and patterns in AMR and AU.

2.2 Sources of data for antimicrobial use and appropriateness of prescribing

Chapter 3 describes patterns and trends in AU, and is based on data collected by four programs:

1. The National Antimicrobial Prescribing Survey (NAPS) is a voluntary online audit performed annually by hospitals to assess antimicrobial prescribing practices and appropriateness of prescribing within the hospital. National data are reported annually. Participating hospitals can interrogate their own data and undertake benchmarking within the audit tool. The methodology for the Hospital NAPS has been varied each year since it started, so results are not directly comparable from year to year.

2. The National Antimicrobial Utilisation Surveillance Program (NAUSP) collects, analyses and reports on AU data at the hospital level. Public and private hospitals voluntarily contribute data throughout each year. Data are published quarterly for states and territories, and hospital peer groups, to support benchmarking. National reports are prepared annually. Participating hospitals can interrogate their own data and generate their own reports at any time.
3. The NPS MedicineWise MedicineInsight program collects data on prescribing in general practice, including prescribing of antimicrobials. Data are provided to participating general practitioners, and reported elsewhere when required.
4. The Pharmaceutical Benefits Scheme (PBS) and Repatriation Pharmaceutical Benefits Scheme (RPBS) allow data collection on antimicrobials dispensed under the PBS/RPBS. For this report, PBS data were obtained from the Australian Government Department of Human Services and the Drug Utilisation Sub Committee which hold long-term historical PBS data.

As part of the overall vision for the national surveillance system, the ANCU has worked to establish effective relationships with these programs and organisations, and, where appropriate, has worked directly with them to establish and build the AURA Surveillance System. Together, these data sources reflect AU and the appropriateness of prescribing in public and private hospitals, and in the community across Australia. Publishing these data and analyses will inform local, and state and territory antimicrobial stewardship programs, and direct more effective strategies to improve prescribing.

2.3 Sources of data for antimicrobial resistance

Chapter 4 describes rates of resistance for priority organisms, and is based on data collected by five programs:

1. The Australian Group on Antimicrobial Resistance (AGAR) collects, analyses and reports on data on priority organisms, including Enterobacteriaceae, *Enterococcus* species, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Acinetobacter* species. Data are reported nationally for three AGAR programs every year.
2. The National Passive AMR Surveillance System (established in collaboration with Queensland Health) uses the OrgTRx system to collect, analyse and report on AMR data from hospitals and private pathology services. Participants include all public hospitals in Queensland, ACT Pathology (Australian Capital Territory), Monash Health (Victoria), the Sydney and South Western Sydney Local Health Districts (New South Wales), SA Pathology (South Australia), Royal Hobart Hospital (Tasmania) and Mater Misericordiae Private Hospitals (Queensland).

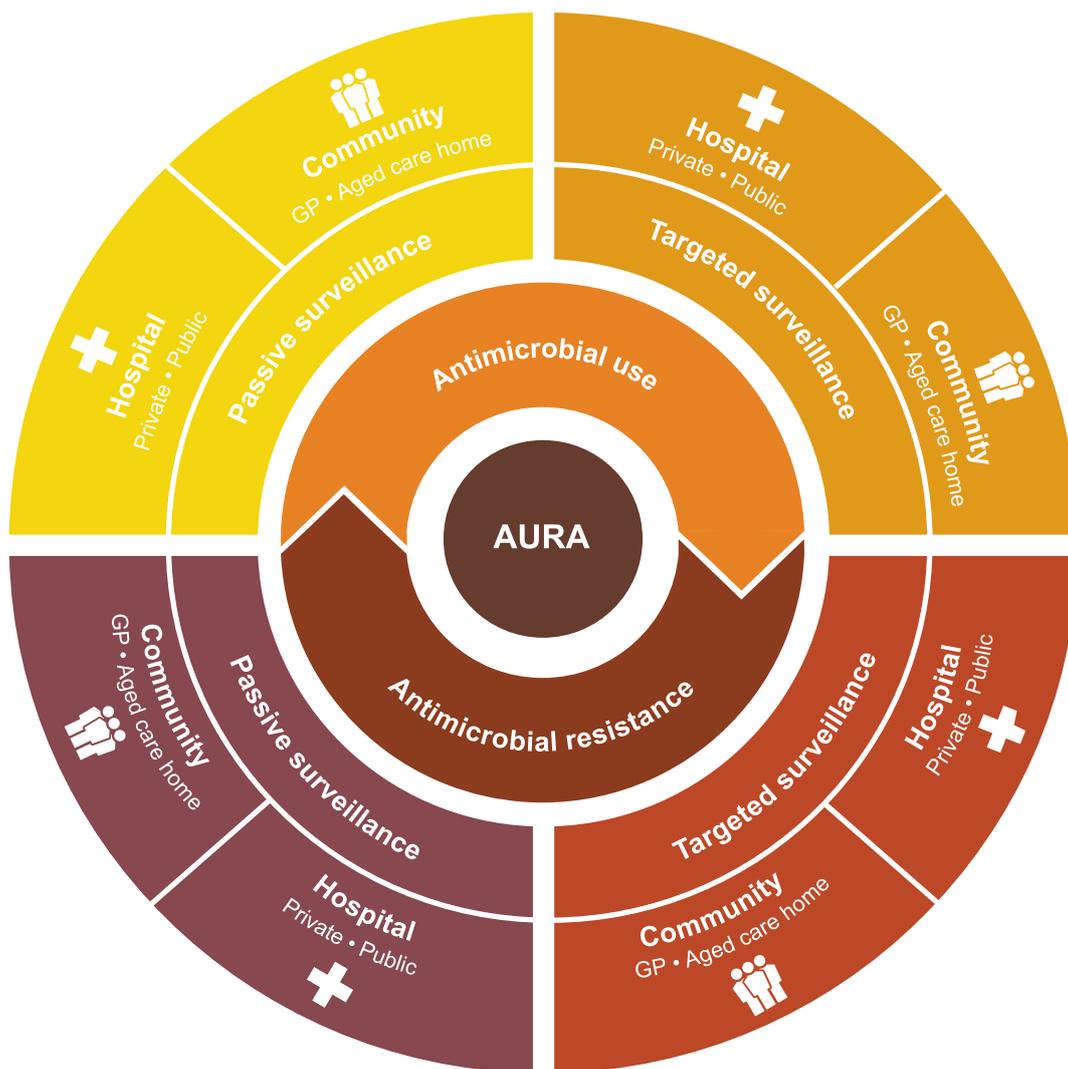
Participants in the National Passive AMR Surveillance System can access their own data and run ad hoc reports within the system to better understand local patterns of resistance. The Commission has been working with all state and territory health authorities, and several private pathology services to achieve national participation and, therefore, national surveillance coverage. It is anticipated that more complete national reporting of AMR data will be available in 2018.
3. The Australian National Neisseria Network (NNN) conducts the national laboratory surveillance programs for *Neisseria gonorrhoeae* and *N. meningitidis*. Data from the NNN programs are published quarterly and annually in the *Communicable Diseases Intelligence* journal.

4. The National Notifiable Diseases Surveillance System (NNDSS) collects data on *Mycobacterium tuberculosis*, and data are published annually in *Communicable Diseases Intelligence*. The Australian Mycobacterium Reference Laboratory Network provides drug susceptibility data on *M. tuberculosis* isolates to state and territory public health units for inclusion in the NNDSS.
5. Sullivan Nicolaides Pathology (SNP) collects data on AMR among organisms in the community, acute facilities and aged care homes, and has worked collaboratively with AURA to provide AMR reports.

Table 2.1 summarises the data sources, the type of surveillance undertaken, the types of data sourced, and the setting and coverage of data included in this report.

Further detail on the data sources for this report, including details of collection methodology, can be found in Appendix 1.

Figure 2.1: Antimicrobial Use and Resistance in Australia (AURA) Surveillance System



GP = general practitioner

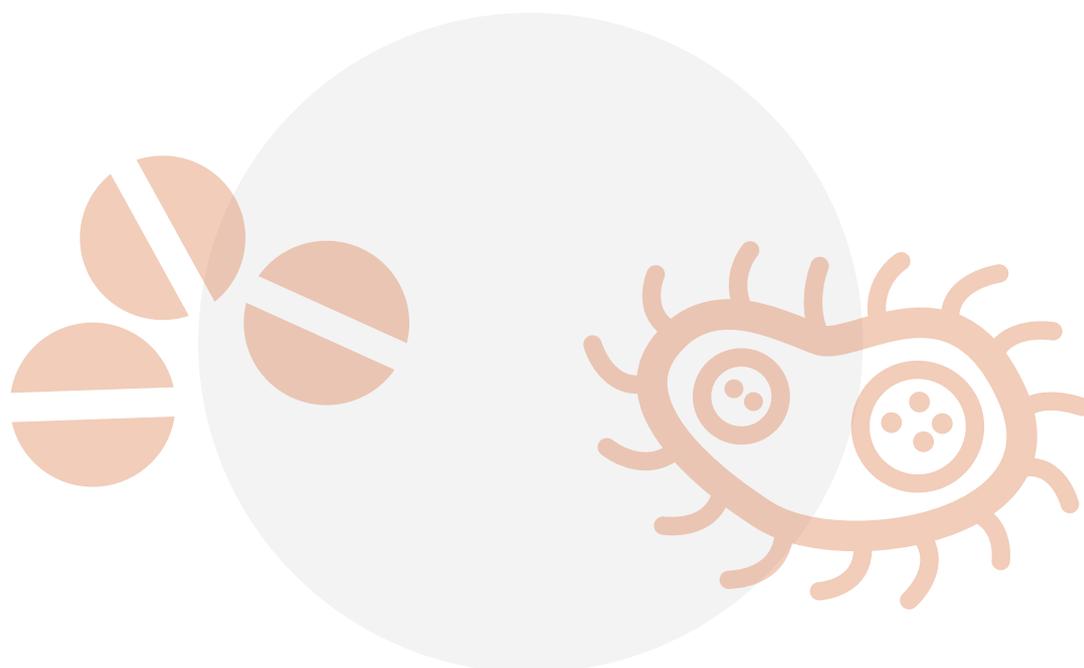
Table 2.1: Data sources for the AURA 2017 report

Subject and type of surveillance	Data source	Type of data	Setting	Coverage
 <ul style="list-style-type: none"> ■ Antimicrobial use ■ Targeted  Community 	MedicineInsight	Appropriateness of prescribing, prescribing pattern	Australian general practice	National (423 general practices, 3.2 million patients)
 <ul style="list-style-type: none"> ■ Antimicrobial use ■ Targeted + Hospital 	National Antimicrobial Prescribing Survey	Appropriateness of prescribing, prescribing volume	Australian public and private hospitals	National (281 hospitals: 213 public and 68 private; 80% of Principal Referral Hospitals; 74.2% of Public Acute Group A Hospitals; 62.2% of Public Acute Group B Hospitals; almost 45% of Private Acute Group A and B Hospitals; 22,021 prescriptions)
 <ul style="list-style-type: none"> ■ Antimicrobial use ■ Passive  Community 	Pharmaceutical Benefits Scheme and Repatriation Pharmaceutical Benefits Scheme	Dispensed volume, trends	Australian general practices and community health services	National (approximately 30 million prescriptions)
 <ul style="list-style-type: none"> ■ Antimicrobial use ■ Passive + Hospital 	National Antimicrobial Utilisation Surveillance Program	Dispensed volume	Australian public and private hospitals	National (159 hospitals: 138 public and 21 private; 100% of Principal Referral Hospitals; almost 85% of Public Acute Group A and B Hospitals)
 <ul style="list-style-type: none"> ■ Antimicrobial resistance ■ Targeted  Community + Hospital 	National Notifiable Diseases Surveillance System	Rates of resistance, trends	Australian general practices and community health services	National (5 reference laboratories)
	National Neisseria Network	Rates of resistance, trends	Australian general practices and community health services	National (9 reference laboratories)
	Australian Group on Antimicrobial Resistance	Rates of resistance, 30-day all-cause mortality	Australian public and private hospitals (community onset)	National (29 laboratories servicing 33 hospitals)
 <ul style="list-style-type: none"> ■ Antimicrobial resistance ■ Targeted + Hospital 	Australian Group on Antimicrobial Resistance	Rates of resistance, 30-day all-cause mortality	Australian public and private hospitals (hospital onset)	National (29 laboratories servicing 33 hospitals)

continued

Table 2.1: continued

Subject and type of surveillance	Data source	Type of data	Setting	Coverage
 <ul style="list-style-type: none"> ■ Antimicrobial resistance ■ Passive 👤 Community 	Sullivan Nicolaides Pathology	Rates of resistance	Queensland and northern New South Wales (community and aged care homes)	Queensland and northern New South Wales
	National Passive AMR Surveillance System (OrgTRx)	Rates of resistance	South Australia (community and aged care homes)	Selected community settings and aged care homes in South Australia
 <ul style="list-style-type: none"> ■ Antimicrobial resistance ■ Passive ⊕ Hospital 	National Passive AMR Surveillance System (OrgTRx)	Rates of resistance	Australian Capital Territory, New South Wales, Queensland, South Australia, Tasmania, Victoria	All Queensland public hospitals; Queensland Mater Misericordiae (selected private hospitals); all public hospitals and private hospitals in South Australia; selected public hospitals and health services in the Australian Capital Territory, New South Wales, Tasmania and Victoria
	Sullivan Nicolaides Pathology	Rates of resistance	Queensland and northern New South Wales	Selected private hospitals in Queensland and northern New South Wales



2.4 Considerations for interpreting the data

The AURA Surveillance System continues to develop the breadth and capacity of AMR and AU surveillance data for the hospital and community sectors. Although this report improves access to a range of data not previously available, several considerations should be noted:

1. Although AMR data are expanding, their availability from the community, including aged care homes, is still limited.
2. Passive surveillance data on AMR in public hospitals are gathered through agreements with the Local Health Networks/Districts or the states and territories. Arrangements are also being progressed with the private sector. These data use the infrastructure provided by the Queensland Health OrgTRx System to analyse and report on AMR data. For 2015, these include data from all public hospitals and health services in Queensland, and selected health services in New South Wales, Victoria, South Australia, Tasmania and the Australian Capital Territory. Discussions are also under way with the Northern Territory and some private sector laboratories. Future reports will therefore represent a greater breadth of AMR data. SA Pathology and ACT Pathology have a significant proportion of AMR data from the community and general practice.
3. AMR data from private hospitals, aged care homes and the community are from SNP through reports specified by AURA, which are integrated with the National Passive AMR Surveillance System data. For 2015, these reports included only data from SNP services in Queensland and northern New South Wales.
4. The AURA Surveillance System has identified *Salmonella* and *Shigella* as priority organisms for surveillance. Data for these organisms are currently being captured through passive surveillance. The expansion of OrgTRx will increase the capacity to review and report on *Salmonella* and *Shigella*.
5. The proportion of prescriptions written in the community that are captured by the PBS/RPBS is estimated to be more than 90%, although the exact percentage is not known. The PBS/RPBS also captures public hospital outpatient and discharge scripts in all states and territories except New South Wales. The PBS/RPBS does not capture data on private scripts or from most Aboriginal and Torres Strait Islander health services.
6. Both NAPS and NAUSP rely on voluntary contribution of data through agreements with the states and territories, and the private sector. The number of contributors continues to expand, and the Commission continues to target areas that could strengthen the data in these programs. Participation in these programs also helps hospitals demonstrate compliance with the Commission's National Safety and Quality Health Service Standards.

At this stage of development of the AURA Surveillance System, although some elements of surveillance can be analysed for trends over time, there are insufficient longitudinal data to undertake time-series analyses across the board. However, the ANCU will continue to increase the inclusion of data from both community and acute sectors, and also historical AMR data, so that trends over time across all sectors can be analysed and reported on.

2.5 Data governance processes

Effective data coordination and management are key components of data governance, which incorporates plans and policies that protect, deliver and strengthen the value of data and information assets. These are essential foundations of the operation of the AURA Surveillance System.

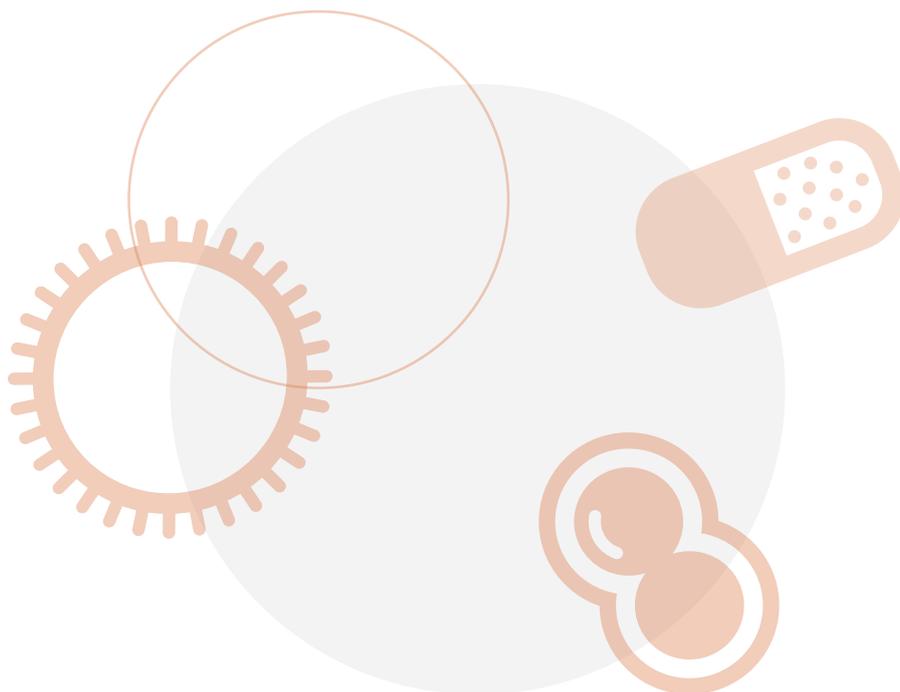
The Commission’s Data Governance Framework provides a structure for the development and implementation of data management policies and provides an overview of data governance arrangements. The framework includes:

- Key data governance concepts, including collection, handling and reporting of data in compliance with legislative, regulatory and policy requirements
- The Commission’s structures and roles to support good data management practices
- Key data management principles
- An overview of policy, guidelines and procedures, including integrated data management.

Data governance is important at every level at which data are created and used. AURA has established several requirements to ensure the integrity and security of the data it uses, as part of its partnership approach and contracting arrangements. These arrangements also ensure that data conform to appropriate standards of data management and quality, and that data are used in accordance with appropriate approvals.

The entities that manage the data collections are the data custodians, and are responsible for:

- Approving access to, and use of, data collections
- Ensuring that data collections are protected from unauthorised access, alteration or loss
- Advising the data users, including any caveats on the use of the data
- Ensuring compliance with relevant legislation and policies regarding administration, quality assurance, and data access and release.



The data collections and systems that form the AURA Surveillance System were originally established for different purposes, such as research, statistical collection and analysis, and health service quality management.

The Commission's data governance arrangements apply to all data requested, collected or funded by the Commission. As a result, each AURA data custodian needs to ensure that data management policies, guidelines and procedures are in place for their collection, including for:

- Data governance
- Data development
- Data acquisition, storage and management
- Data security
- Data quality management
- Data processing
- Data disclosure and reporting
- Metadata management.

The Commission continues to work with each of its partners and contracted suppliers of data, and reports to improve standardisation of data definitions, comparability of data items, development of new data items and analytical methodologies. The Commission will also continue to identify opportunities to reduce duplication of, and effort associated with, data systems and provision of data by health services, and to increase the utility of the systems.



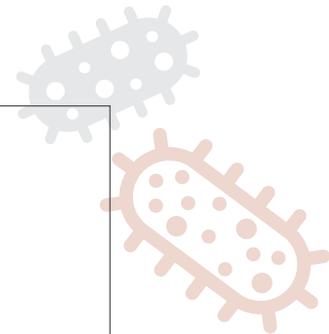
Chapter 3

Antimicrobial use and appropriateness

Key messages

Hospitals

- Antibacterial use in Australian hospitals has continued to decline since the peak usage rate in 2010 – there was a 2.1% decrease in 2015 compared with 2014, down from 936 defined daily doses (DDDs) per 1,000 occupied bed days (OBDs) to 916.4 DDDs per 1,000 OBDs.
- Antibacterial use varies between and within states and territories, from a mean of 1,220 DDDs per 1,000 OBDs in Tasmania to 763 DDDs per 1,000 OBDs in Western Australia.
- The antibacterial classes with the greatest variation are aminoglycosides and antipseudomonal penicillin combinations, but there is insufficient evidence to fully explain the reasons for the variation.
- Consistent with 2014, the five most commonly used antimicrobials were amoxicillin–clavulanate, cefazolin, amoxicillin, flucloxacillin and doxycycline. Together, they accounted for 49% of antibacterial use.
- Although the antibacterial usage rate has declined, the prevalence of antimicrobial use (AU) increased from 38.4% of patients being prescribed an antimicrobial in 2014 to 40.5% in 2015.
- Overall, 21.9% of prescriptions were assessed as inappropriate, and 23.3% were not compliant with guidelines, compared with 23.0% and 24.3%, respectively, in 2014.
- The most common indications for prescribing antimicrobials were surgical prophylaxis (15.5%), community-acquired pneumonia (10.5%), medical prophylaxis (7.6%), sepsis (5.7%) and urinary tract infection (5.0%).
- Improvement in the proportion of surgical prophylaxis prescriptions extending beyond 24 hours duration continued, from 41.8% in 2013 to 27.4% in 2015.



- The continuing high rate of inappropriate prescribing of cefalexin since 2013 – almost 40% in 2015 – is a concern and will be an area of focus for improvement activities. Most inappropriate use of cefalexin occurs for surgical prophylaxis, urinary tract infection and pneumonia.

Community

- In 2015, systemic AU remained high – 45% of the Australian population was supplied at least one systemic antibiotic through the Pharmaceutical Benefits Scheme/ Repatriation Pharmaceutical Benefits Scheme.
- The rate of prescribing in the community increased from 23.8 DDDs per 1,000 inhabitants per day in 2014 to 25.4 DDDs per 1,000 inhabitants per day in 2015.
- The most commonly supplied systemic antimicrobials were amoxicillin, cefalexin and amoxicillin-clavulanate.
- Around 14% of amoxicillin-clavulanate prescribing was for upper respiratory tract infections, where antimicrobials were not indicated, and 15% was for sinusitis, where antimicrobials are only indicated in specific circumstances.
- Of patients who presented to a general practitioner for colds and other upper respiratory tract infections, 60% had an antimicrobial prescribed where no indication was recorded.
- A large proportion of antimicrobials prescribed were not those recommended by *Therapeutic Guidelines: Antibiotic*.
- Prescribing varies across states and territories, between major cities and other regions, and across socioeconomic groups; however, it is not yet possible to identify the factors that are driving geographic patterns of antimicrobial prescribing in Australia.
- Australia’s antimicrobial prescribing rate is the eighth highest among member countries of the Organisation for Economic Co-operation and Development, and is more than double that of countries that prescribe the lowest rate of antimicrobials.

Antimicrobial use (AU) is a key factor in the development of antimicrobial resistance (AMR) – the more antimicrobials are used, the more likely it is that resistance will develop. Sometimes antimicrobials are prescribed inappropriately, such as using antibacterials to treat a viral infection, or prescribing antimicrobials either when they are not indicated or for longer than necessary. Surveillance of AU and appropriateness of prescribing is essential to inform prevention and containment strategies for AMR.

This chapter provides data and analyses of AU, dispensing, and appropriateness of prescribing in public and private hospitals and in the community.

3.1 Antimicrobial use in hospitals

An integral part of improving surveillance of AU in Australia is the collaboration with two significant programs in Australia to provide hospital data on the volume of antimicrobials dispensed and the appropriateness of prescribing. As part of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System, the National Antimicrobial Utilisation Surveillance Program (NAUSP) conducted by SA Health and the National Antimicrobial Prescribing Survey (NAPS) conducted by the National Centre for Antimicrobial Stewardship have been strengthened to collect, analyse and report on data about AU and appropriateness

of prescribing. These reports have contributed to informing antimicrobial stewardship (AMS) programs and improving prescribing practice.

Data on the volume of antibacterial use in this report have been obtained from the 2015 NAUSP report²⁰ and from additional analyses. NAUSP data are drawn from 159 Australian acute care hospitals (138 public and 21 private hospitals), and were collected between January and December 2015. The NAUSP data collection now includes all Principal Referral Hospitals, and more than 80% of all Public Acute Group A and Public Acute Group B Hospitals.

AURA 2017 includes historical comparisons, comparisons of data between and within states and territories, and comparisons of usage rates between hospital peer groups for selected classes.²⁰ Rates are expressed as defined daily doses (DDDs) per 1,000 occupied bed days (OBDs) (see Box 3.1). Hospitals are classified into peer groups according to the November 2015 Australian Institute of Health and Welfare criteria.²¹

Participating hospitals contribute to NAUSP on a voluntary basis, and all states and territories are represented in the program. NAUSP does not include data for children because DDDs have not been defined for them.

● Box 3.1: Defined daily doses

A defined daily dose (DDD) is the average daily adult maintenance dose of a medicine for its main indication.²⁴ DDDs for most antibacterials are included in the J01 class of the World Health Organization's (WHO's) uniform classification index of medicines.* The DDD is widely accepted in international surveillance programs because it enables comparison of antibacterial use within and between countries. Antibacterial use in hospitals is usually measured as a rate: the DDD divided by a denominator of clinical activity within the hospital, such as the number of occupied bed days (OBDs) or the number of patient days.

Sales or prescription data about medicine use in the community can be shown as DDDs per 1,000 inhabitants per day to give a population estimate for use of a medicine (or group of medicines). For example, 10 DDDs per 1,000 inhabitants per day means that, on a given day, 1% of the population received a medicine (or group of medicines). This estimate is useful for medicines that treat chronic illnesses for which the DDD and the average prescribed daily dose (PDD) are similar.

What are some other measures of medicine use?

A medicine's DDD may or may not be the same as the medicine's PDD for a particular person (based on individual characteristics such as weight or kidney function) or its recommended daily dose (RDD) as found in guidelines. For example, the DDD for ampicillin is 2,000 mg, and a PDD could be 750–3,000 mg (depending on the indication, severity of infection and kidney function). In one guideline, the RDD to treat a liver abscess is 8,000 mg.^{23,24}

An individual annual estimate of use can be shown as DDDs per inhabitant per year. This gives an estimate of the number of days for which an individual received the medicine (or group of medicines) per year. For example, 10 DDDs per inhabitant per year implies that, on average, during that year, each inhabitant received 10 days of treatment with that medicine (or group of medicines).

● **Box 3.1:** continued

In some international jurisdictions, DDDs per 100 bed days are used to give a hospital-wide estimate of the rate of use of a medicine (or a group of medicines). This allows benchmarking, because rate is independent of hospital size. However, different hospitals and, indeed, different countries define bed days differently. For accuracy, bed day figures should be adjusted for beds that are occupied.[†]

An alternative to the DDD is days of therapy (DOT). The DOT is the sum of days in which each medicine is given.²⁵ For example, 28 days of ciprofloxacin + 15 days of ceftriaxone + 15 days of azithromycin = 58 DOTs per 100 patient days. Measuring DOT requires individual patient data to sum the total dose of all medicines given (therefore, it does not reflect the dose of individual medicines).²⁵

One comparative analysis measured overall antibacterial use by DDD or DOT for 50 antibacterials prescribed for adults discharged from 130 hospitals in the United States during the 12 months ending 31 July 2003.²⁶ For antibacterials for which the dose given was similar to the DDD (for example, linezolid), estimates of use based on the DDD and the DOT were similar. In contrast, for antibacterials for which the dose given was larger than the DDD (for example, cefipeme), estimates of use based on the DDD were larger than estimates of use based on the DOT. Similarly, for antibacterials for which the dose given was smaller than the DDD (for example, ceftriaxone), estimates of use based on the DDD were smaller than estimates of use based on the DOT.

Another comparative analysis showed the same three-fold increase in the DDD and the DOT for antifungal use in a paediatrics and

obstetrics–gynaecology during the same 10-year period.²⁷

What are some limitations of a DDD?

A DDD does not account for patient variability, hospital infection rates or casemix. For example, the relative proportions of erythromycin use as an antibacterial and for gastric motility are unknown. In addition, DDDs are not suitable for measuring antimicrobial use in paediatrics.

A DDD does not measure the dose given or an individual’s exposure to a medicine (or group of medicines). For some antibacterials, DDDs do not align with common hospital PDDs: a DDD is usually calculated for oral treatment and is often lower than a PDD for intravenous treatment. For example, the DDD for oral flucloxacillin is 2,000 mg, but a PDD used for intravenous flucloxacillin in hospitals can be four-fold higher, at 8,000 mg.

A DDD does not measure appropriate prescribing. For example, prescribing a broad-spectrum antibacterial such as piperacillin–tazobactam to treat intra-abdominal sepsis is 1 DDD. A more common choice to prescribe a combination of three older antibacterials such as amoxicillin, gentamicin and metronidazole is 5 DDDs.

* J01 is one code within the Anatomical Therapeutic Chemical (ATC) classification system of alphanumeric codes developed by WHO for the classification of medicines and other medical products. The ATC code J01 is applied to the group within this classification system of medicines labelled ‘Antibacterials for systemic use’.

† In Australia, occupied bed days is the total number of hospital inpatient bed days during the period of interest (for example, a month), taken from a count of the number of hospital inpatients every day at about midnight.

Data on appropriateness of prescribing were drawn from *Antimicrobial Prescribing Practice in Australian Hospitals: Results of the 2015 Hospital National Antimicrobial Prescribing Survey*, conducted between September 2015 and February 2016.²² These data identify areas where prescribing varies from guidelines – either *Therapeutic Guidelines: Antibiotic*²³ or locally endorsed guidelines.

A total of 281 hospitals (213 public and 68 private) participated in the 2015 Hospital NAPS, a 13% increase in participation compared with 2014.²² Principal Referral Hospitals were well represented (80%), as were Public Acute Group A and Public Acute Group B Hospitals (74% and 62%, respectively), and Women's and Children's Hospitals (71%). Participation was lower from Public and Private Acute Group C Hospitals; the Commission will continue to work with state and territory health authorities and the private sector to improve participation by these hospitals. Data were compared with those collected in 248 hospitals in 2014 and 151 hospitals in 2013. Participation in the Hospital NAPS is voluntary.

Because the NAUSP reports are confined to analyses of use of systemic antibacterials in Australian hospitals, the term 'antibacterial' is used when referring to the output of analyses of the NAUSP data, and when comparisons are made with data reported by other countries. Analyses of NAPS data also include analyses of appropriateness of prescribing of antifungals and antivirals.

This report uses therapeutic groupings that accord with the World Health Organization Anatomical Therapeutic Chemical (ATC) system (see *AURA 2017: Supplementary data*).

Volume of use in hospitals

Total annual usage rates

The total-hospital antibacterial usage rate for all NAUSP contributors ($n = 159$) was 916 DDDs per 1,000 OBDs (Figure 3.1). This is a 2.1% decrease from 2014. The median annual usage rate was 936 DDDs per 1,000 OBDs, and the mean usage rate across the 159 hospitals was 957 DDDs per 1,000 OBDs (range 322–1808 DDDs per 1,000 OBDs).

Figure 3.1 shows that Australia's antibacterial use in hospitals peaked in 2010, and has decreased gradually since then. There has been a sustained decrease in antimicrobial use in hospitals that have contributed continuously to NAUSP between 2010 and 2015. The annual aggregate antibacterial usage rates by antibacterial class are also shown.

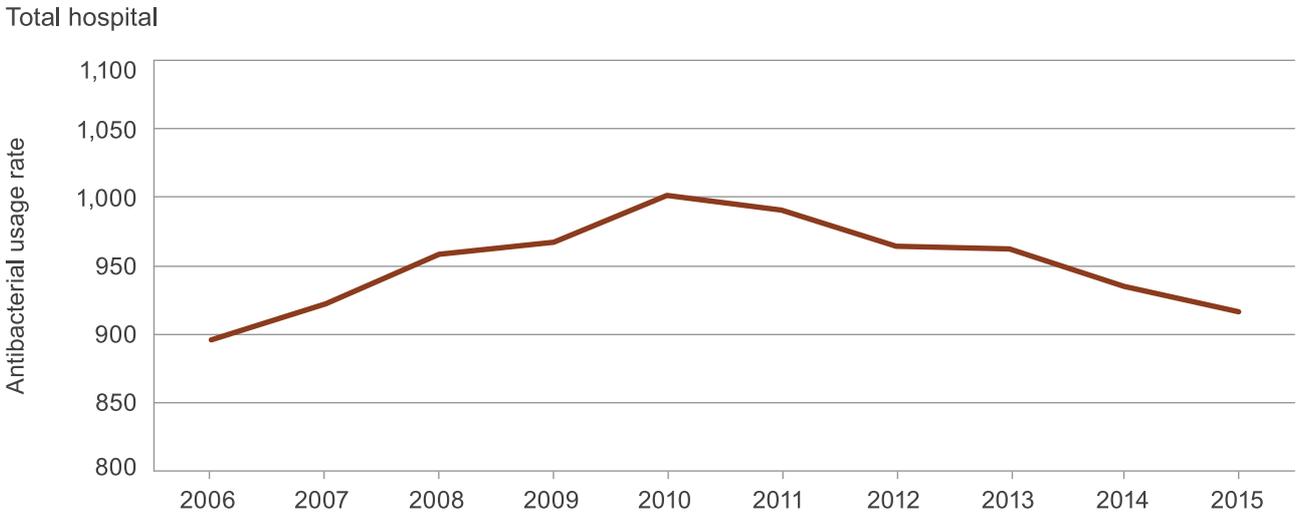
Australia's antibacterial use in hospitals peaked in 2010, and has decreased gradually since then.

Most commonly used antibacterials

Twenty antibacterials accounted for 93% of all those used in Australian hospitals, based on DDDs per 1,000 OBDs (Figure 3.2). Six antibacterials – amoxicillin–clavulanate, cefazolin, amoxicillin, flucloxacillin, doxycycline and cefalexin – represented 54% of antibacterials used in NAUSP contributor hospitals. The same usage pattern was reported in the 2014 NAUSP annual report.²⁸ Ten antibacterials accounted for 72.4% of use.

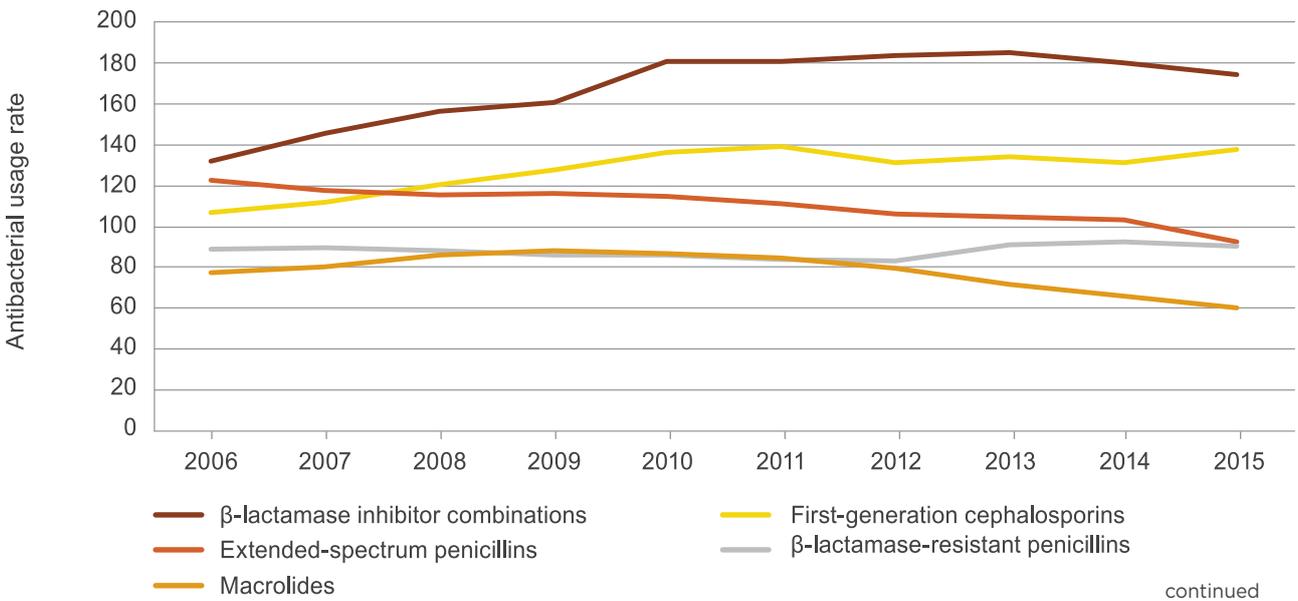
A change in ranking occurred between 2015 and 2014 – cefazolin moved from being the third most frequently used antibacterial to the second. This may reflect updated recommendations for dosing in surgical prophylaxis, with cefazolin doses increasing from 1 gram to 2 grams for many surgical procedures.²³

Figure 3.1: Annual aggregate antibacterial use in NAUSP contributor hospitals (DDD/1,000 OBD), 2006–2015



Source: NAUSP²⁰

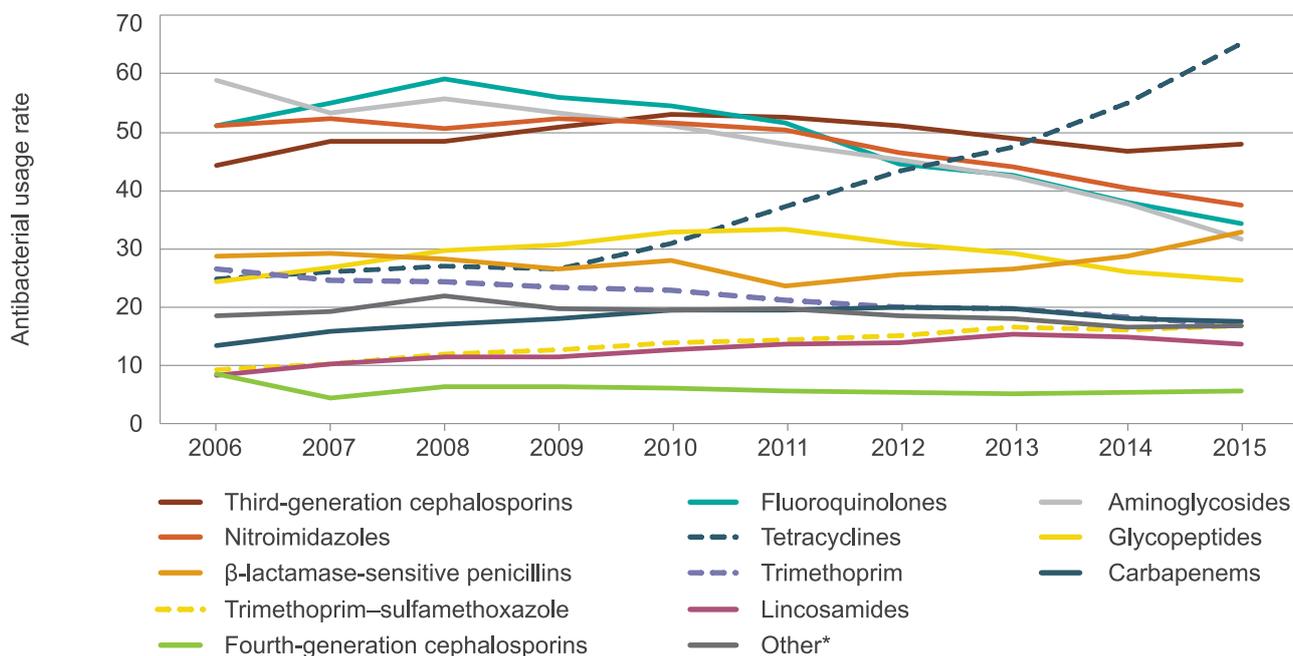
Five most commonly used antibacterial classes



Note: The five antibacterial classes represent more than 60% of antibacterials used in NAUSP contributor hospitals from 2006 to 2015.

Figure 3.1: continued

Other antibacterial classes



* 'Other' comprises amphenicols, monobactams, nitrofurans, other antibacterials (linezolid and daptomycin), other cephalosporins and penems (ceftaroline), polymyxins, rifamycins, second-generation cephalosporins, steroids (fusidic acid), streptogramins and streptomycins.

Note: Other antibacterial classes combined account for less than 40% of the antibacterials used in NAUSP contributor hospitals from 2006 to 2015.

Source: NAUSP²⁰

Twenty antibacterials accounted for 93% of all antibacterials used in Australian hospitals.

Highly reserved antibacterials accounted for very small percentages of total use – for example, linezolid (0.12%), daptomycin (0.12%) and colistin (0.07%).

Nine of the top 10 antibacterials reported in NAPS also appear in the NAUSP top 10 antibacterials used (Table 3.1).

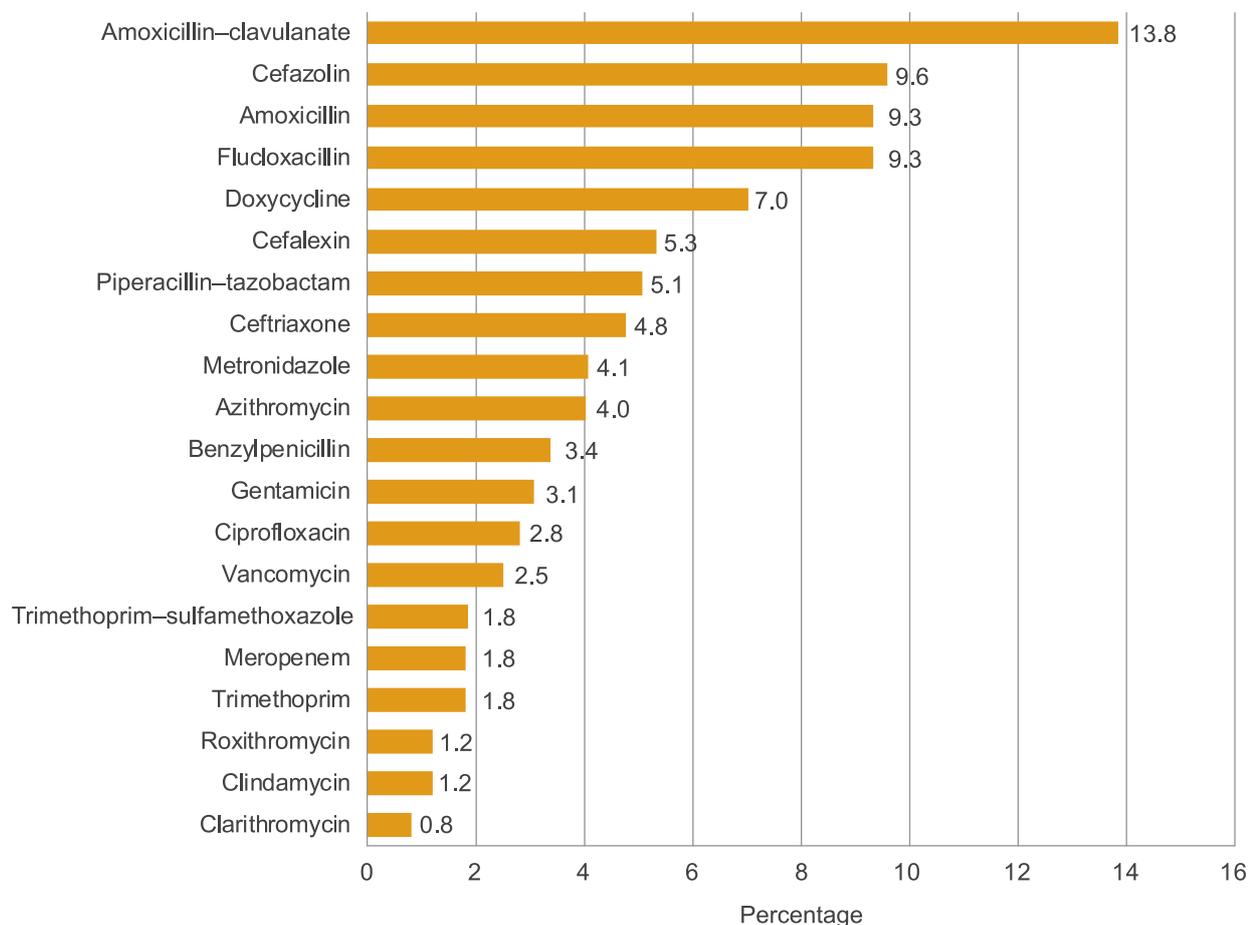
Antibacterial usage rates by state and territory

Aggregated annual total-hospital antibacterial usage rates for NAUSP contributors for 2015 are shown by state and territory in Figure 3.3.

States and territories vary in the number of contributing hospitals and the proportion of these that are private hospitals. *AURA 2017: Supplementary data* provides a breakdown of the categories of hospitals.

There was large variation in antibacterial classes used and aggregate usage rates between states and territories. Tasmania had the highest rate of 1,225 DDDs per 1,000 OBDs, and Western Australia had the lowest rate of 767 DDDs per 1,000 OBDs – a difference of 458 DDDs per 1,000 OBDs (Figure 3.3).

Figure 3.2: Top 20 antibacterials as a percentage of all antibacterials used in NAUSP contributor hospitals, 2015



Source: NAUSP²⁰

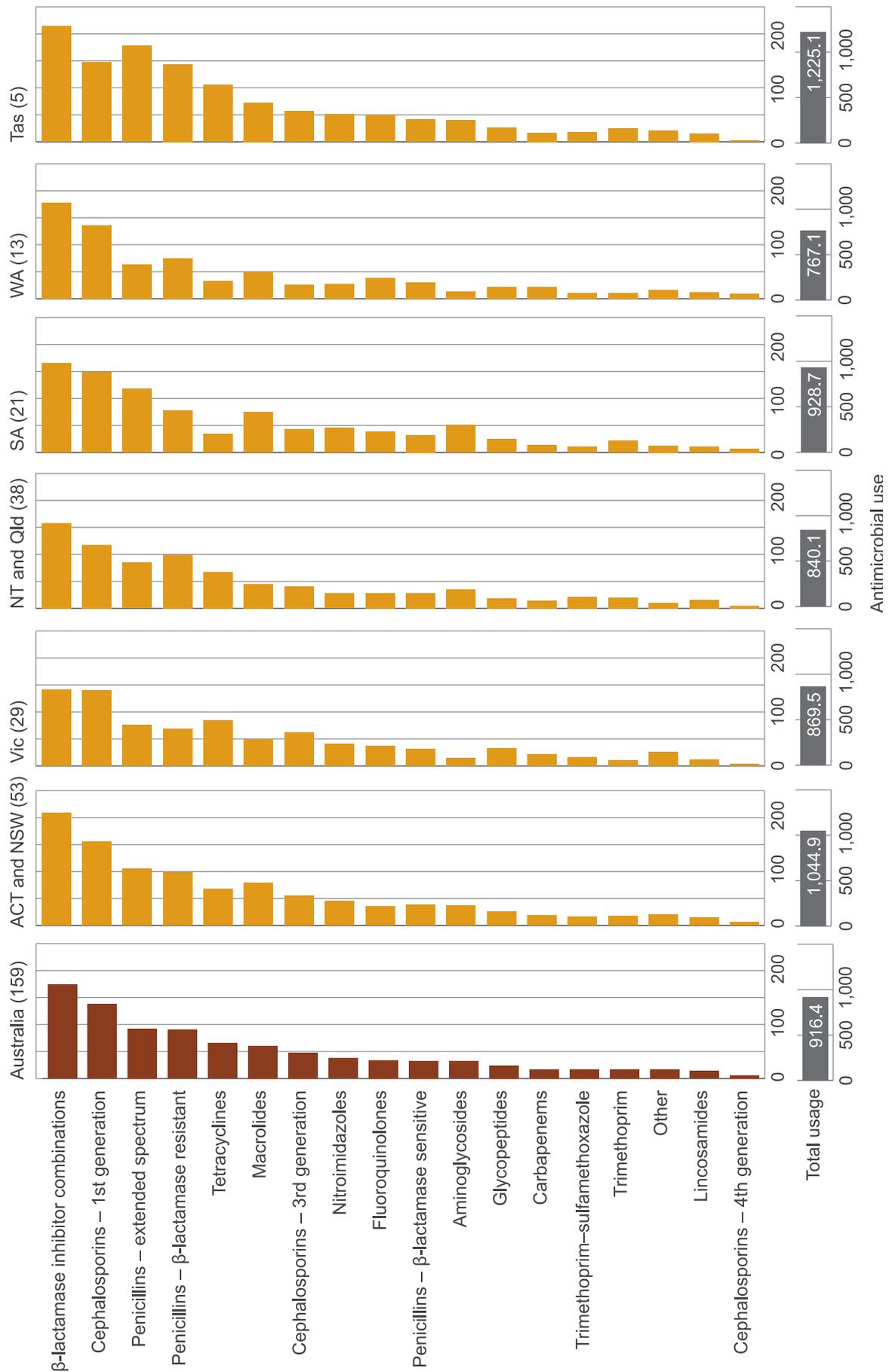
Table 3.1: Most frequently prescribed and supplied antibacterials, as reported by NAPS and NAUSP, 2015

Rank	Most frequently prescribed (NAPS)	Most frequently supplied (NAUSP)
1	Cefazolin (13.6%)	Amoxicillin-clavulanate (13.8%)
2	Ceftriaxone (9%)	Cefazolin (9.6%)
3	Metronidazole (6.5%)	Amoxicillin (9.3%)
4	Amoxicillin-clavulanate (6.3%)	Flucloxacillin (9.3%)
5	Piperacillin-tazobactam (6.3%)	Doxycycline (7.0%)
6	Cefalexin (5.0%)	Cefalexin (5.3%)
7	Flucloxacillin (4.1%)	Piperacillin-tazobactam (5.1%)
8	Doxycycline (4.0%)	Ceftriaxone (4.8%)
9	Amoxicillin (3.5%)	Metronidazole (4.1%)
10	Gentamicin (3.2%)	Azithromycin (4.0%)

Sources: NAPS²² and NAUSP²⁰



Figure 3.3: Overall antibacterial usage rates (DDD/1,000 OBD) in hospitals, by state and territory, 2015



Note: Numbers of hospitals include public, private and Specialist Women's Hospitals.
Source: NAUSP²⁰

● From information to action

Benchmarking antimicrobial use in Tasmania: the need to investigate the data in relation to defined daily doses

The Tasmanian Health Service (THS) provides care to approximately 500,000 Tasmanians, and coordinates antimicrobial stewardship (AMS) activities across its services. The THS has four major Acute Public Hospitals:

- Royal Hobart Hospital (RHH), a Principal Referral Hospital with 450 beds
- Another large Acute Public Hospital with 300 beds
- Two regional (small public) hospitals with a total of 260 beds.

Both RHH and the large hospital have comprehensive AMS programs supported by on-site infectious diseases services and dedicated infectious diseases pharmacists. The regional hospitals do not have on-site infectious diseases services, but AMS support is provided remotely by RHH.

In AURA 2016, data from the National Antimicrobial Utilisation Surveillance Program (NAUSP) showed that THS hospitals had an aggregate antimicrobial usage rate in 2014 of 1,354 defined daily doses (DDDs) per 1,000 occupied bed days (OBDs), with a range of 1,182-1,552 DDDs per 1,000 OBDs. This rate was the highest in the country and above the national average of 933 DDDs per 1,000 OBDs. Because of the small number of hospitals and differences in casemix compared with the

mainland states, direct comparisons between states should be interpreted with caution.

RHH had a usage rate of 1,182 DDDs per 1,000 OBDs, which was higher than the national peer rate for Principal Referral Hospitals of 920 DDDs per 1,000 OBDs. RHH provides comprehensive services, including intensive care (adults and paediatric/neonatal), haematology-oncology, cystic fibrosis, neurosurgery and cardiothoracic surgery.

RHH has been contributing antimicrobial usage data to NAUSP since 2004 (Figure A).

RHH launched its AMS program in May 2009. Antimicrobial usage rates decreased from 1,293 DDDs per 1,000 OBDs in 2009-10 to 1,025 DDDs per 1,000 OBDs in 2012-13, but then increased. This increase occurred even though the AMS program was maintained and the regular NAUSP reports, detailing the use of 'broad-spectrum antibiotics' and comparing it with use among peer group members, had been reviewed without significant concern. Surveys continued to demonstrate appropriateness of antimicrobial prescribing that was consistent with national comparators - the whole-of-hospital survey undertaken at RHH for the 2015 National Antimicrobial Prescribing Survey (NAPS) showed that, overall, 76.3% of antimicrobial prescriptions were appropriate, compared with the national average of 74.6%.

continued

● From information to action: continued

Figure A: Royal Hobart Hospital antimicrobial usage data (DDD/1,000 OBD), 2004-05 to 2014-15

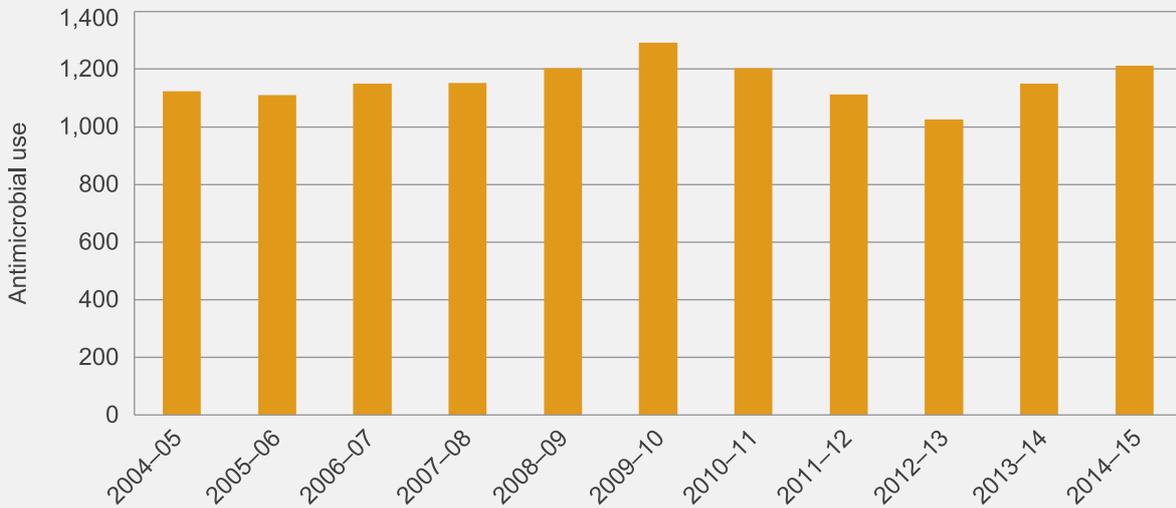
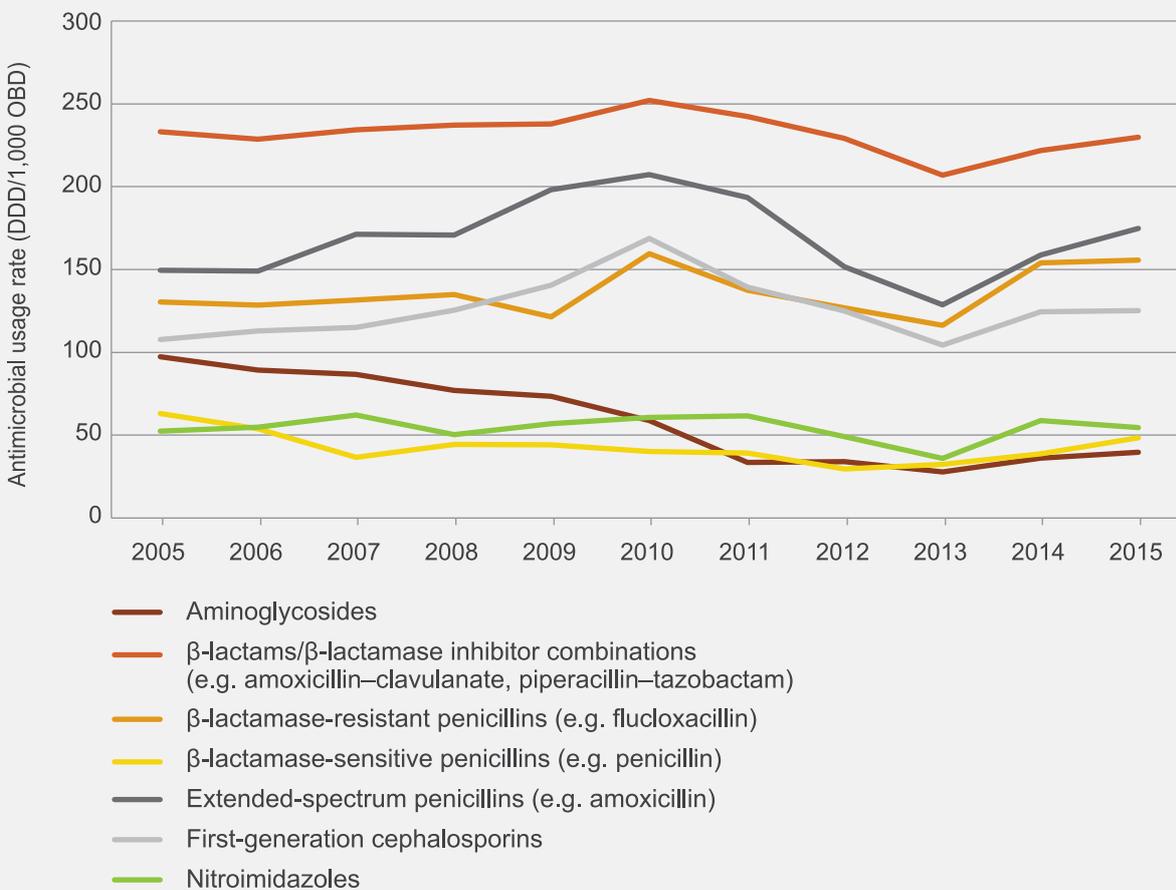


Figure B: Antimicrobial classes whose use increased by at least 10 DDD/1,000 OBD between 2012-13 and 2014-15



continued

● **From information to action:** continued

To understand why the total antimicrobial use (AU) was increasing, RHH reviewed its pattern of use for each antimicrobial class. Figure B shows all the antibiotic classes whose use had increased by at least 10 DDDs per 1,000 OBDs between 2012-13 and 2014-15. The sum of the increases for these classes was 175 DDDs per 1,000 OBDs. Other than the class of β -lactam/ β -lactamase inhibitor combinations, they were all narrow-spectrum agents.

The increasing use of these classes coincided with two important changes to antimicrobial prescribing at RHH. First, the hospital implemented new guidelines for antibiotic therapy for intra-abdominal infections in general surgery patients to align with the latest revision of *Therapeutic Guidelines: Antibiotic* in 2014 (version 15). This included the following changes:

- Conventional triple antimicrobial therapy (amoxicillin, metronidazole and gentamicin) was recommended for most patients
- The recommended dose of intravenous (IV) amoxicillin was doubled from 1 gram every 6 hours to 2 grams every 6 hours

- When gentamicin was contraindicated, IV piperacillin-tazobactam (rather than IV ceftriaxone) was recommended for empirical therapy for perforated viscus, severe or complicated diverticulitis, or ascending cholangitis
- The recommended oral de-escalation agent was amoxicillin-clavulanate (where there was no contraindication).

Examples of how these changes affected DDDs are shown in Table A.

The second important change to prescribing that occurred during this time was a change in the standard cefazolin dosing for surgical antibiotic prophylaxis from weight-based dosing (that is, 1 gram for patients <80 kilograms and 2 grams for patients \geq 80 kilograms) to 2 grams for all adult patients, regardless of weight. This recommendation is consistent with *Therapeutic Guidelines: Antibiotic*, and equates to an average increase of 0.3 DDDs for each 2-gram dose of cefazolin.

Table A: Defined daily doses (DDD) for hypothetical examples of intra-abdominal infections in an 80-kilogram adult

Example therapy	DDD for each agent	Total DDD
<ul style="list-style-type: none"> • 1 g ceftriaxone daily • 500 mg metronidazole every 12 hours 	<ul style="list-style-type: none"> • Ceftriaxone = 0.5 • Metronidazole = 0.7 	1.2
Standard recommendation in <i>Therapeutic Guidelines: Antibiotic</i> and RHH guidelines: <ul style="list-style-type: none"> • 2 g amoxicillin every 6 hours • 500 mg metronidazole every 12 hours • 5 mg/kg/day gentamicin 	<ul style="list-style-type: none"> • Amoxicillin = 8 • Metronidazole = 0.7 • Gentamicin = 1.7 	10.4
4.5 g tazocin IV every 8 hours	0.96	0.96
4.5 g tazocin IV every 6 hours	1.3	1.3

IV = intravenous; RHH = Royal Hobart Hospital

continued

● From information to action: continued

Together, these data indicate that the increased use of narrow-spectrum agents as a result of updated guidelines contributed to the increase in AU at RHH. This highlights the limitations of using DDDs as the sole measure of a facility's AU, as well as the potential limitations of using DDDs per 1,000 OBDs for benchmarking. Ongoing surveillance of AU remains an important component of a comprehensive AMS program and continues to be a priority for the THS.

Understanding AU is complex. Although measuring and monitoring usage rates is

essential, it is only one part of the overall picture of an organisation's AU. If monitoring or benchmarking identifies potential discrepancies, or marked changes over time, this should trigger further investigation. In this case, changes in hospital guidelines contributed to a large change in use without any decrease in appropriateness. By combining data from the different Antimicrobial Use and Resistance in Australia programs – in this case, NAUSP and NAPS – local AMS teams can better understand their hospitals' patterns of AU to improve patient care.

Table 3.2 lists the aggregate antibacterial usage rates by state and territory; Australian Institute of Health and Welfare public hospital peer group; and private hospitals, excluding Women's and Children's Hospitals. Data for states and territories with a small number of contributing hospitals should be viewed with caution, because the data may not be representative. New South Wales and the Australian Capital Territory had the broadest range of DDDs per 1,000 OBDs between hospitals. More information on interstate comparisons of usage data can be found in the NAUSP annual report.²⁰

Usage rates of carbapenems are low nationally (see *AURA 2017: Supplementary data*) and possibly influenced by prescribing preferences in particular hospitals because they have a broad spectrum and are reserved for treatment of infections caused by multidrug-resistant organisms. Meropenem is the main carbapenem used in NAUSP contributor hospitals, possibly because of its lower incidence of neurotoxicity and superior activity against *Pseudomonas* species compared with other carbapenems. Meropenem has become a key reserve-line antibacterial because it can be used to treat

infections with extended-spectrum β -lactamase-producing microorganisms, which are increasing in incidence.

As expected, carbapenem usage rates reported by NAUSP contributors were highest in Principal Referral Hospitals, followed by Public Acute Group A and Public Acute Group B Hospitals. Use in Public Acute Group C Hospitals was minimal.

Figures 3.4–3.7 show the differing patterns of use among states and territories of individual antibacterials in the four therapeutic classes that are most likely to drive antimicrobial resistance (AMR): aminoglycosides, third- and fourth-generation cephalosporins, fluoroquinolones and macrolides.

Gentamicin is the aminoglycoside used most often, along with amikacin and tobramycin. Although there is some variation in use, rates have steadily decreased during the past five years across all states and territories, with large variations between them (Figure 3.4). This may reflect changes in recommendations on gentamicin use in *Therapeutic Guidelines: Antibiotic*, or increasing concerns about ototoxicity.²⁹ Amikacin and tobramycin usage

Table 3.2: Antibacterial usage rates in NAUSP contributor hospitals, by state and territory, and peer group, 2015

State or territory	Hospitals contributing to NAUSP (number)	All hospitals rate (DDD/1,000 OBD)	All hospitals range (DDD/1,000 OBD)	Principal Referral Hospitals (DDD/1,000 OBD)	Public Acute Group A Hospitals (DDD/1,000 OBD)	Public Acute Group B Hospitals (DDD/1,000 OBD)	Public Acute Group C Hospitals (DDD/1,000 OBD)	Private Hospitals (DDD/1,000 OBD)
ACT and NSW	53	1,079.0	416-1,792	988.7 (n = 12)	1,113.2 (n = 22)	1,133.2 (n = 15)	1,001.3 (n <5)	-
Vic	29	887.0	322-1,524	837.4 (n = 6)	962.1 (n = 11)	843.9 (n = 7)	-	848.7 (n <5)
NT and Qld	38	916.0	378-1,808	810.7 (n = 6)	846.8 (n = 12)	664.9 (n = 7)	1,453.1 (n = 5)	981.8 (n = 7)
SA	21	873.0	341-1,445	1,011.8 (n <5)	886.2 (n <5)	840.1 (n <5)	724.6 (n <5)	856.7 (n = 7)
WA	13	763.0	392-1,139	924.1 (n <5)	508.3 (n <5)	894.6 (n = 2)	-	873.1 (n <5)
Tas	5	1,220.0	1,183-1,254	-	1,212.5 (n <5)	-	-	-
Australia	159	954.1	322-1,808	914.4 (n = 30)	939 (n = 55)	872.7 (n = 36)	984.9 (n = 12)	917.4 (n = 21)

- = data not able to be calculated because of either a small sample size or no contributors

Note: Rates are mean rates for all hospitals. Specialist Women’s Hospitals are not included. Private hospitals are combined because of small numbers.

Source: NAUSP²⁰

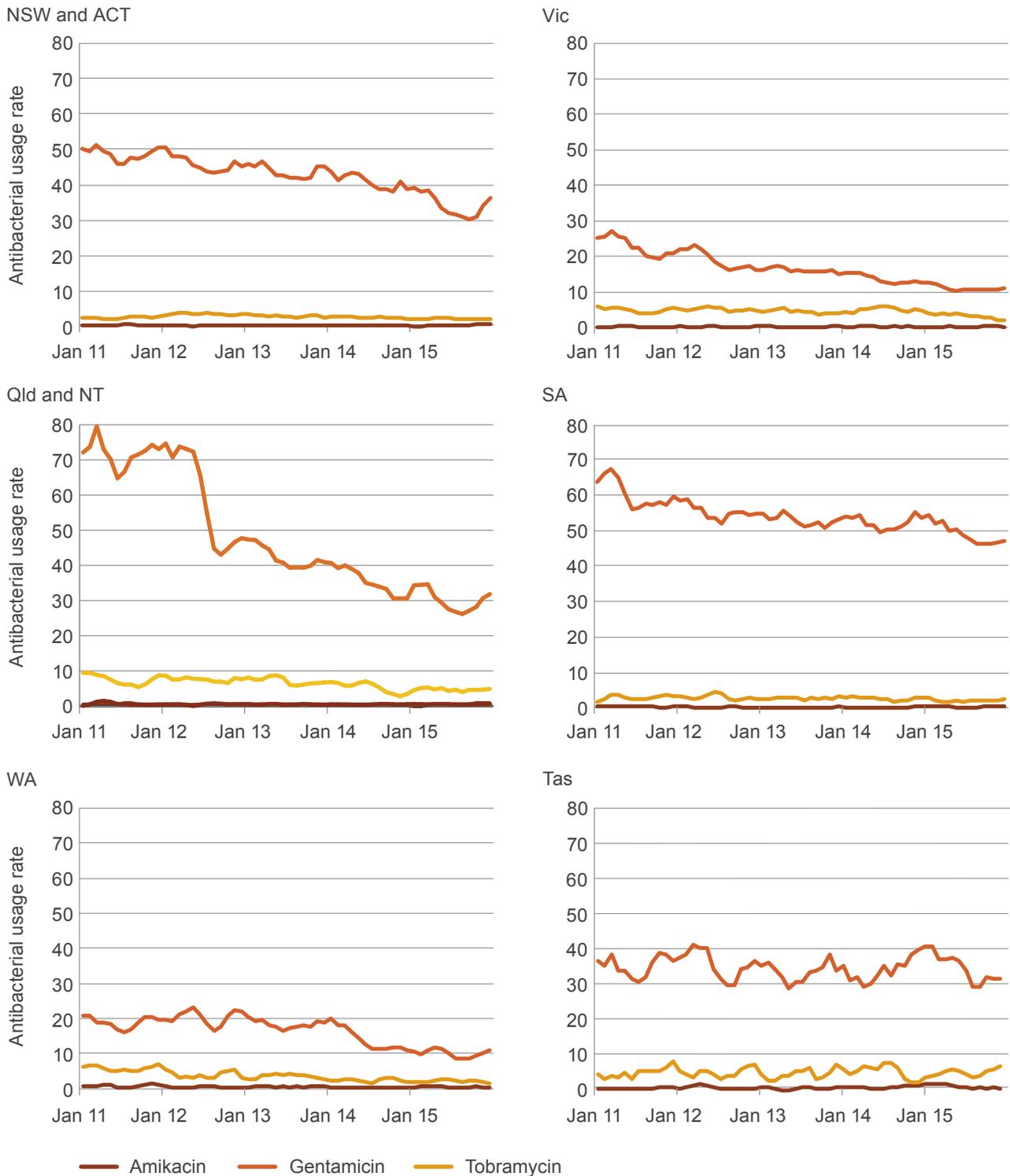
rates remain low compared with those of gentamicin. Amikacin and tobramycin are more expensive than gentamicin, and are reserved for specific indications. Higher usage rates of tobramycin appear to be confined to larger hospitals with referral services for people with cystic fibrosis, who are at increased risk of lung infections caused by *Pseudomonas aeruginosa*.

Rates of gentamicin use have steadily decreased during the past five years in all states and territories.

Ceftriaxone, a third-generation cephalosporin, shows a pattern of seasonal use, reflecting its role in the treatment of lower respiratory tract infections, which peak in the winter months (Figure 3.5). Usage rates of ceftriaxone are lower in Western Australia than in other states and territories. Investigating use of other antibacterials that are used instead of ceftriaxone may help to explain this variation.

Ceftriaxone, a third-generation cephalosporin, shows a pattern of seasonal use, reflecting its role in the treatment of lower respiratory tract infections, which peak in the winter months.

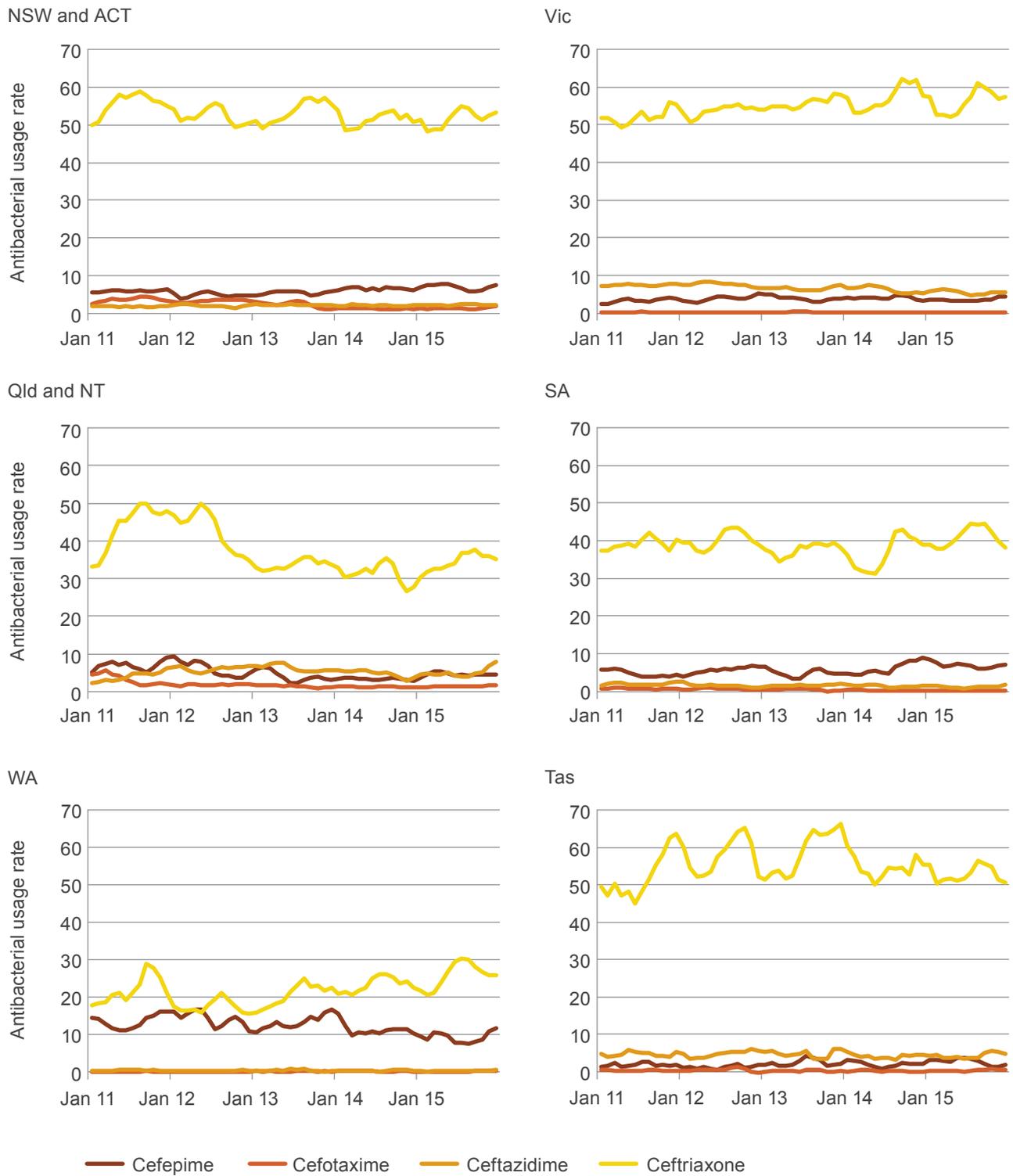
Figure 3.4: Aminoglycoside usage rates (DDD/1,000 OBD) in NAUSP contributor hospitals, by state and territory, 2011-2015 (3-month moving average)



Note: Tobramycin usage rates include inhaled formulations.

Source: NAUSP²⁰

Figure 3.5: Cephalosporin usage rates (DDD/1,000 OBD) in NAUSP contributor hospitals, by state and territory, 2011–2015 (3-month moving average)



Source: NAUSP²⁰

● From information to action

Targeting high-use areas to improve antimicrobial stewardship

In the 2014-15 National Antimicrobial Utilisation Surveillance Program (NAUSP), one Principal Referral Hospital identified itself as having a total-hospital antimicrobial usage rate that was similar to the average for the peer group (Figure A), but an intensive care unit (ICU) rate that was the second highest in the peer group (Figure B). Antimicrobial use in the ICU was higher across most antimicrobial classes, despite twice-weekly multidisciplinary infectious diseases rounds that had been in place for many years. Information on these findings was escalated through the hospital's standard health service risk management processes and identified as a high-risk issue for action.

A scoping study identified that approximately two-thirds of broad-spectrum antimicrobial use was attributed to a handful of indications and problems with the duration of surgical prophylaxis. Many antimicrobial review opportunities were missed in the time between the twice-weekly meetings.

The study informed changes to antimicrobial review processes in the ICU. Meetings were restructured to separate the patients who

required more complex infectious diseases consultation from the general ICU-led reviews. Meeting frequency was increased to three times a week, and the focus was changed to common ICU prescribing syndromes and surgical prophylaxis. A further change resulted in the antimicrobial stewardship physician facilitating these meetings.

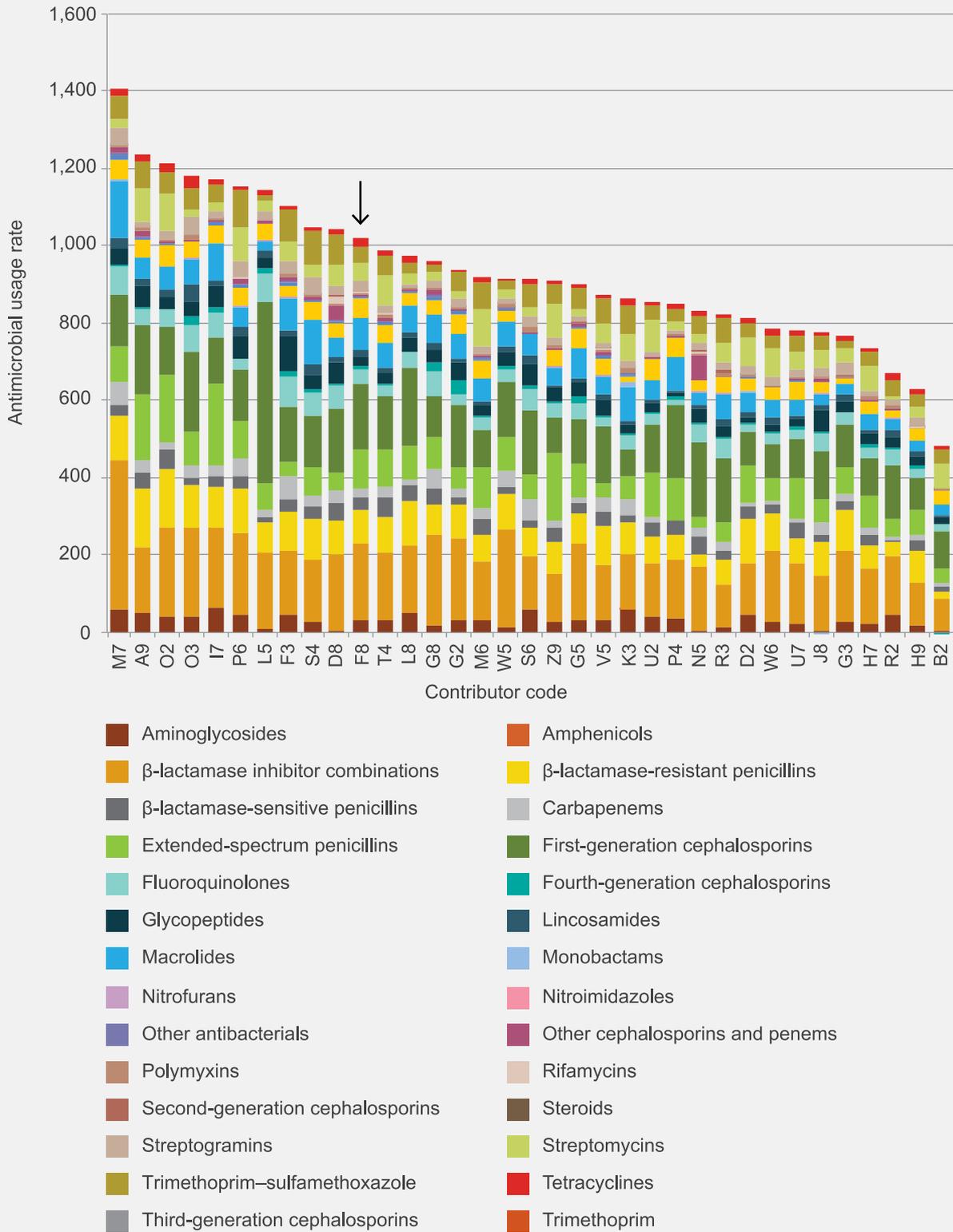
The first target for improvement – a 15% reduction in meropenem use within one year – was based on a combination of study findings and high rates of carbapenemase-producing Enterobacteriaceae in the ICU.

Monitoring of meropenem use, using the NAUSP portal, demonstrated a 35% seasonally comparable reduction in meropenem use at six months. Increases in the use of other agents were seen, but not at the rates expected for direct switches from carbapenems. No episodes of 'recommendations not followed' were found after the second month of implementation of the changes. The annual point prevalence study in 2016 (using the National Antimicrobial Prescribing Survey platform) showed an absolute reduction of 29% in surgical prophylaxis continuing for longer than 24 hours within three months of implementing the changes.

continued

● From information to action: continued

Figure A: Annual antimicrobial usage rate (DDD/1,000 OBD) in the Principal Referral Hospital (indicated by an arrow) for total-hospital use, 2014-15

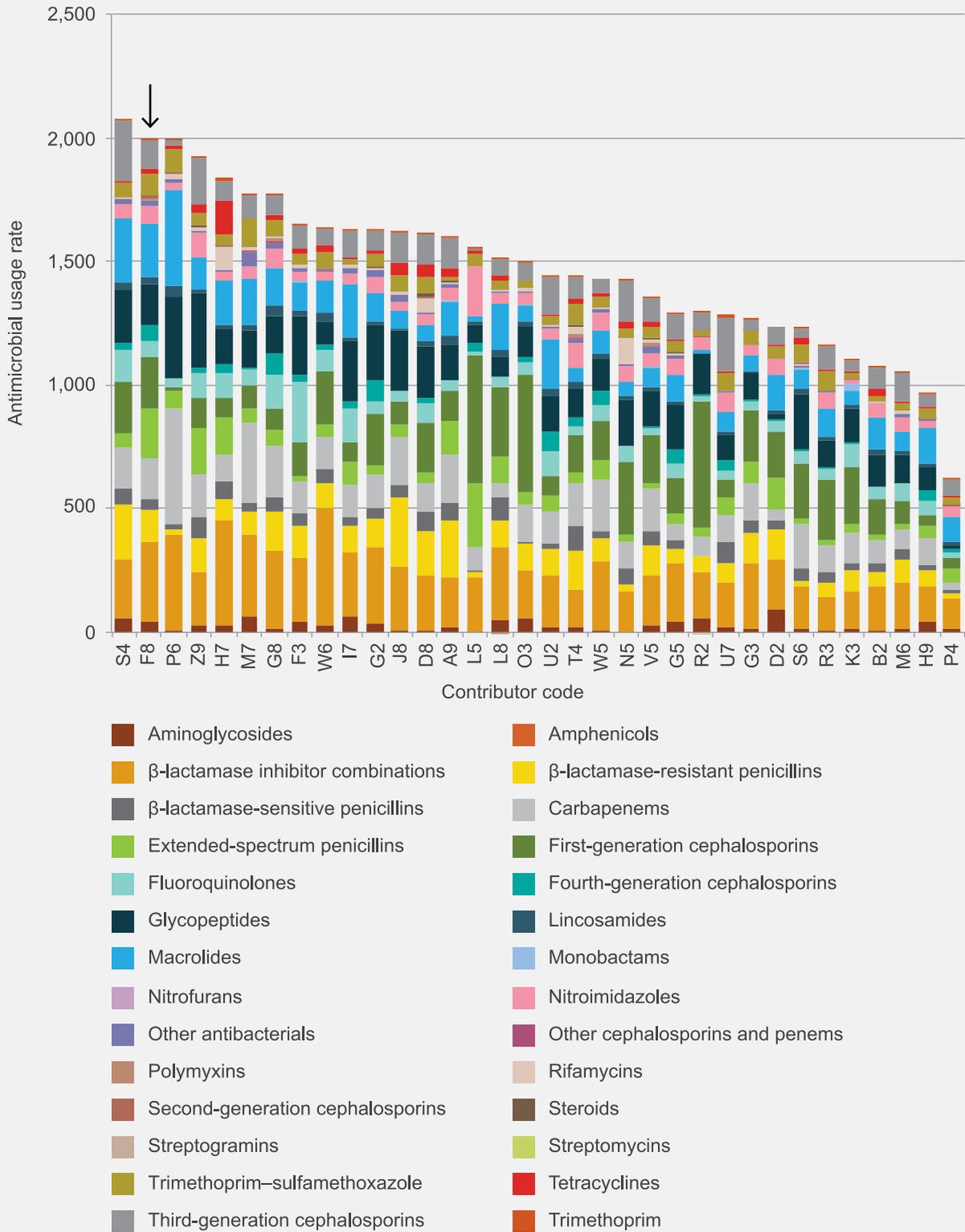


continued



● From information to action: continued

Figure B: Annual antimicrobial usage rate (DDD/1,000 OBD) in the Principal Referral Hospital (indicated by an arrow) for ICU use, 2014-15

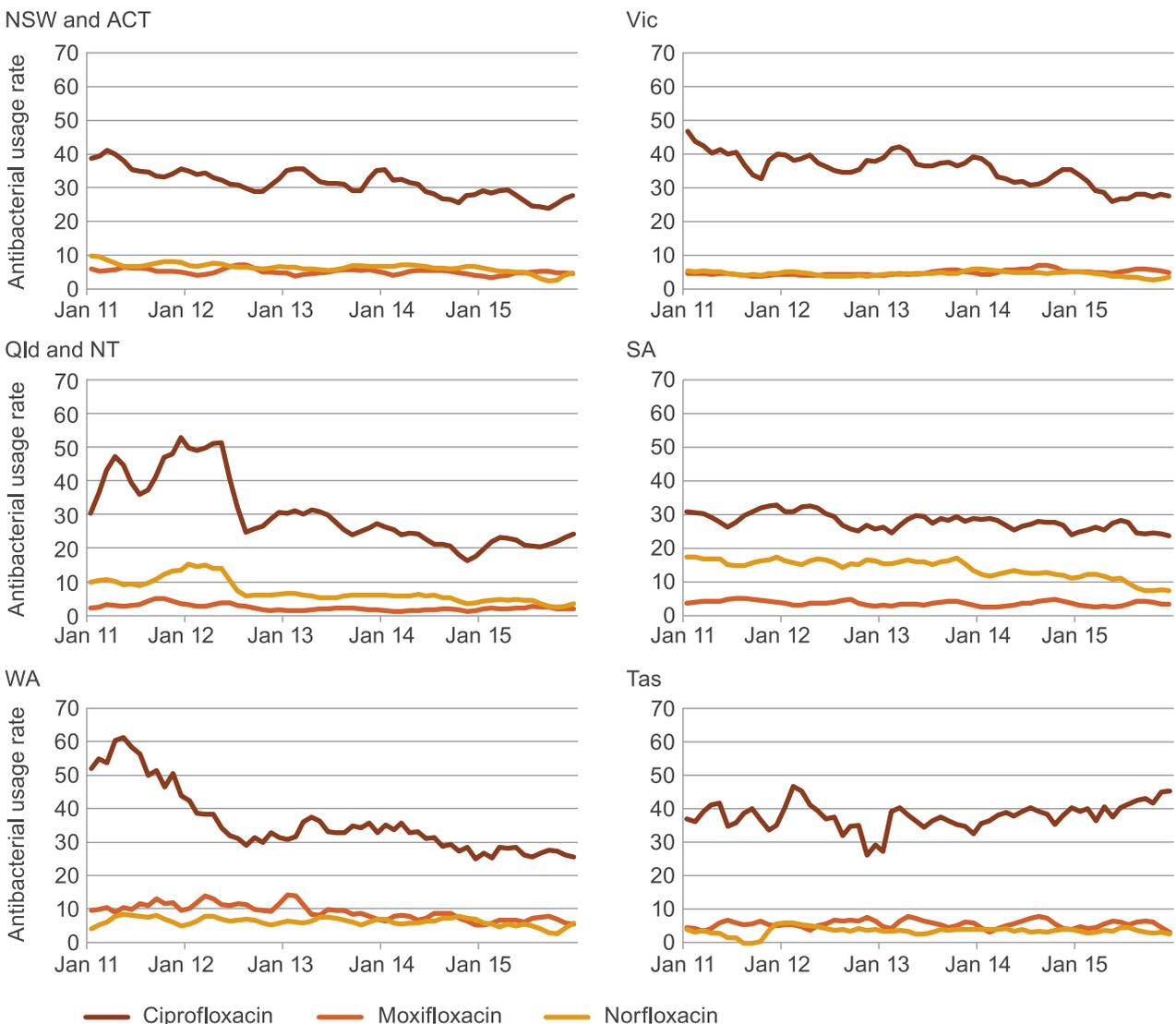


Fluoroquinolone usage rates have decreased since 2011 (Figure 3.6). Most Australian hospitals and formularies restrict their use, because they are a reserved antimicrobial for treatment of infections that are resistant to other agents³⁰ and there are few indications for which a fluoroquinolone is the first-line treatment.²³ Ciprofloxacin is the fluoroquinolone used most often. Usage rates of norfloxacin and moxifloxacin have remained relatively constant, probably because there are few indications for which they are a first-line treatment.

Ciprofloxacin is the fluoroquinolone used most often.

Usage rates for the macrolides azithromycin and roxithromycin show a marked seasonal variation; use peaks in the winter months because they are used to treat atypical organisms in community-acquired pneumonia (Figure 3.7). There is variation in usage rates between hospitals, which may be explained by differences in hospital restrictions for some macrolides (for example, azithromycin) or differences in prescribing

Figure 3.6: Fluoroquinolone usage rates (DDD/1,000 OBD) in NAUSP contributor hospitals, by state and territory, 2011–2015 (3-month moving average)



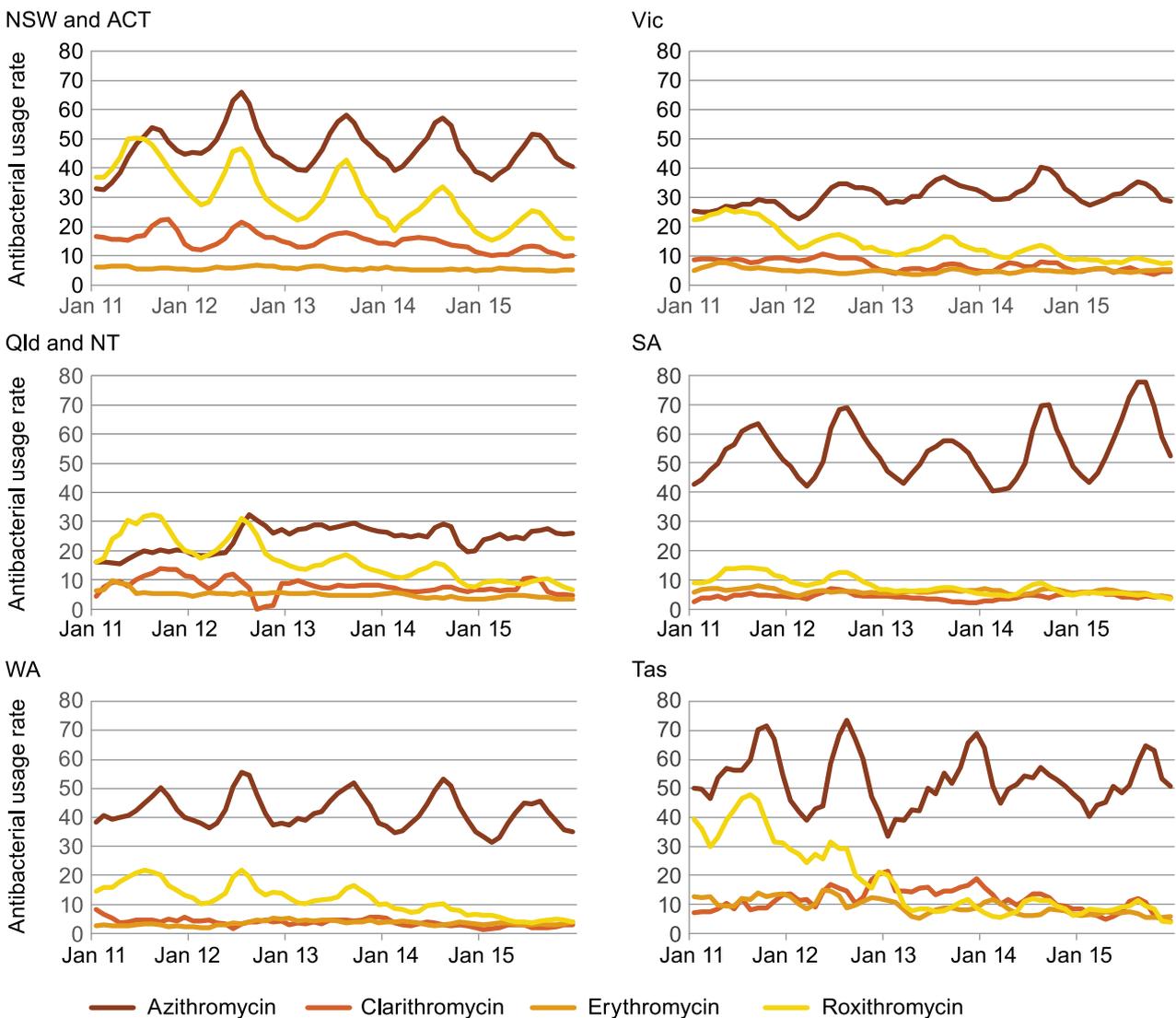
Source: NAUSP²⁰

protocols for respiratory tract infections (for example, community-acquired pneumonia). Azithromycin is the macrolide used most often in NAUSP contributor hospitals, possibly because of its wide spectrum of activity and low likelihood of interaction with other medicines. It is unclear what proportion of erythromycin use is for gastric motility rather than as an antibacterial because NAUSP does not collect data about indications.

Usage rates for the macrolides azithromycin and roxithromycin peak in the winter months, because of their role in treating community-acquired pneumonia.

More information on interstate comparisons of usage data for other antibacterial classes such as the carbapenems, glycopeptides, penicillin-β-lactamase inhibitor combinations and reserve-line antibacterials can be found in *AURA 2017: Supplementary data* and the 2015 NAUSP report.²⁰

Figure 3.7: Macrolide usage rates (DDD/1,000 OBD) in NAUSP contributor hospitals, by state and territory, 2011–2015 (3-month moving average)



Source: NAUSP²⁰

● From information to action

Monitoring fluoroquinolone use through MedTRx and NAUSP

MedTRx is a Queensland Health IT system designed to monitor antimicrobial use (AU) for all Queensland Health public hospitals. MedTRx data are reported to the National Antimicrobial Utilisation Surveillance Program (NAUSP). NAUSP has been operating since 2004, and is an important element to support antimicrobial stewardship (AMS). By contributing data to NAUSP, Queensland Health hospitals can compare their AU with other hospitals in the same peer group, identify areas for improvement and inform their AMS programs.

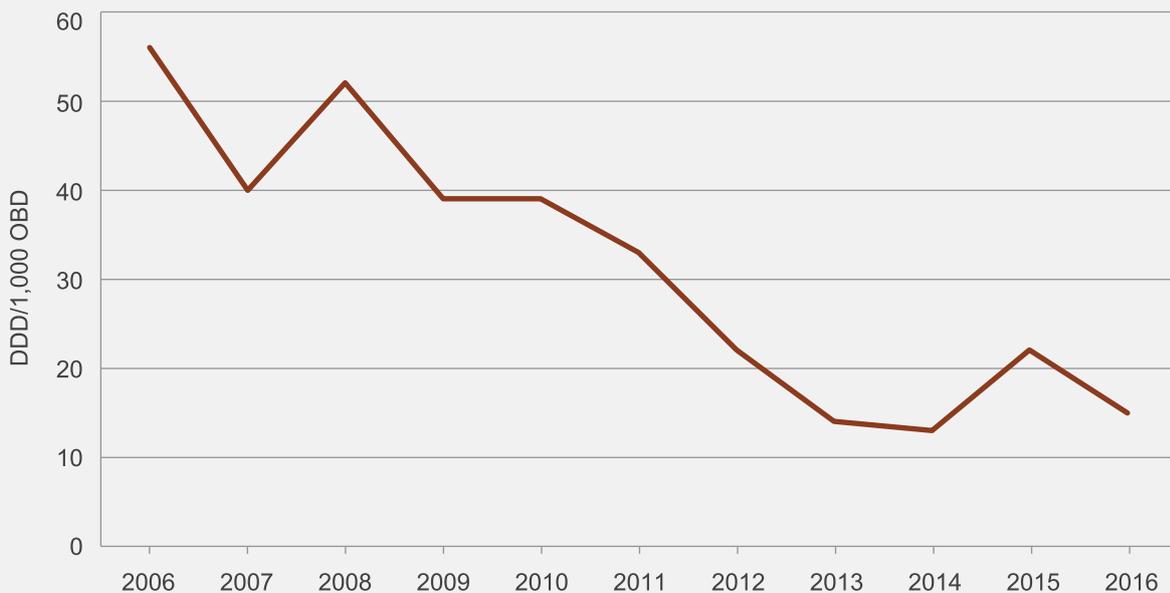
A large secondary referral hospital in northern Queensland offers a comprehensive range of health services and has been submitting data on AU to MedTRx since 2006. The hospital's earliest MedTRx data in 2006 showed

high use of fluoroquinolone antimicrobials, at 56 defined daily doses (DDDs) per 1,000 patient days. In 2008, this was 52 DDDs per 1,000 patient days (Figure A).

MedTRx software allows reports and graphs to be produced from a wide range of data sources with a multitude of parameters. Hospitals can directly access MedTRx data, and the data that are submitted to NAUSP are benchmarked against peer hospitals across Australia. Both MedTRx and NAUSP data are available to the AMS team in this hospital.

The hospital used its MedTRx and NAUSP data to promote the benefits of infectious diseases specialists, and in 2011 it was successful in recruiting additional staff. MedTRx data were also used to provide feedback to hospital clinicians about variations in practices, and to explore options for more prudent use of fluoroquinolones.

Figure A: The hospital's decreasing trend for prescription of fluoroquinolones, 2006–2016



Source: Hospital data from MedTRx

continued

● From information to action: continued

The hospital implemented closer monitoring and control of prescription of antimicrobials that require approval from the infectious diseases unit.

Since 2006, with closer monitoring, the hospital's use of fluoroquinolones has steadily declined; by 2011, it had decreased to 33 DDDs per 1,000 patient days. By 2014, the hospital had achieved the lowest fluoroquinolone usage rate in Queensland, at 13 DDDs per 1,000 patient days. The AMS team continues to monitor fluoroquinolone use, which remains low, and also feeds back benchmarked data from NAUSP to prescribers (including regularly to the intensive care unit) to assist in continually improving prescribing practice.

Antimicrobial use by hospital peer group

Classifying hospital data by peer group allows each hospital to compare its data with similar hospitals, to identify variations in use and areas for improvement. In the future, AURA and NAUSP surveillance data can be used to evaluate the effectiveness of interventions to improve prescribing and use.

Private hospitals were included with public hospitals of similar size and patient mix for the analyses. Data from four Women's Hospitals were not included in these analyses because of low numbers.

Aminoglycoside usage rates show downwards trends in each peer group in 2011–2015 (see Figure 3.8). In 2015, usage rates in Principal Referral, Public Acute Group A and Public Acute Group B Hospitals were similar. The small number of contributors in the Public Acute Group C Hospital cohort means that it is not possible to comment on the trend in these smaller

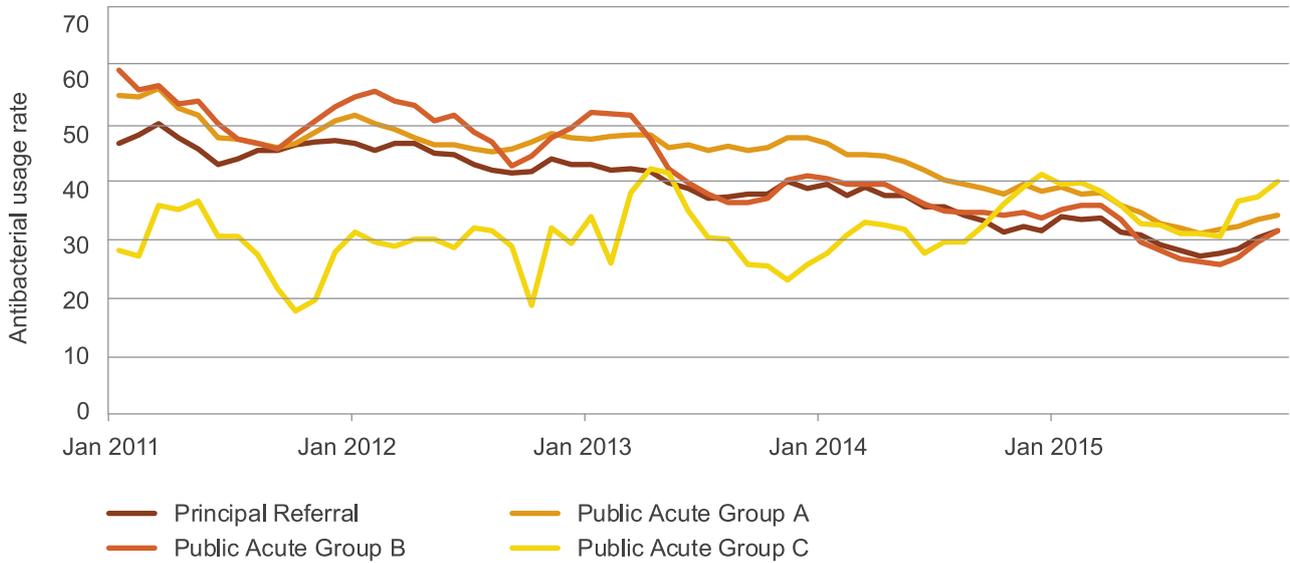
facilities. Gentamicin is the aminoglycoside used most in Australia and is widely used as initial empirical therapy.

Usage rates of third- and fourth-generation cephalosporins were similar in all four peer groups (Figure 3.9). Although NAUSP data do not assess appropriateness of prescribing, in general, greater usage of broad-spectrum cephalosporins would be expected in larger hospitals. Reviewing hospital-level data could show whether use in hospitals other than those in the Principal Referral Hospital peer group was appropriate. The 2015 Hospital NAPS reported that about 40% of ceftriaxone prescriptions were inappropriate.²² The reasons most often given for inappropriate use of ceftriaxone for respiratory tract infections were that the spectrum was too broad and an antimicrobial was not indicated.²²

Usage rates of fluoroquinolones in NAUSP contributor hospitals declined from 2011 to 2015 (Figure 3.10). The greatest decline occurred in Principal Referral Hospitals. Usage rates for Public Acute Group C Hospitals are lower than for other peer groups, and do not show a downwards trend as seen for the other peer groups. In 2015, usage rates of fluoroquinolones were similar in Public Acute Group A, B and C Hospitals.

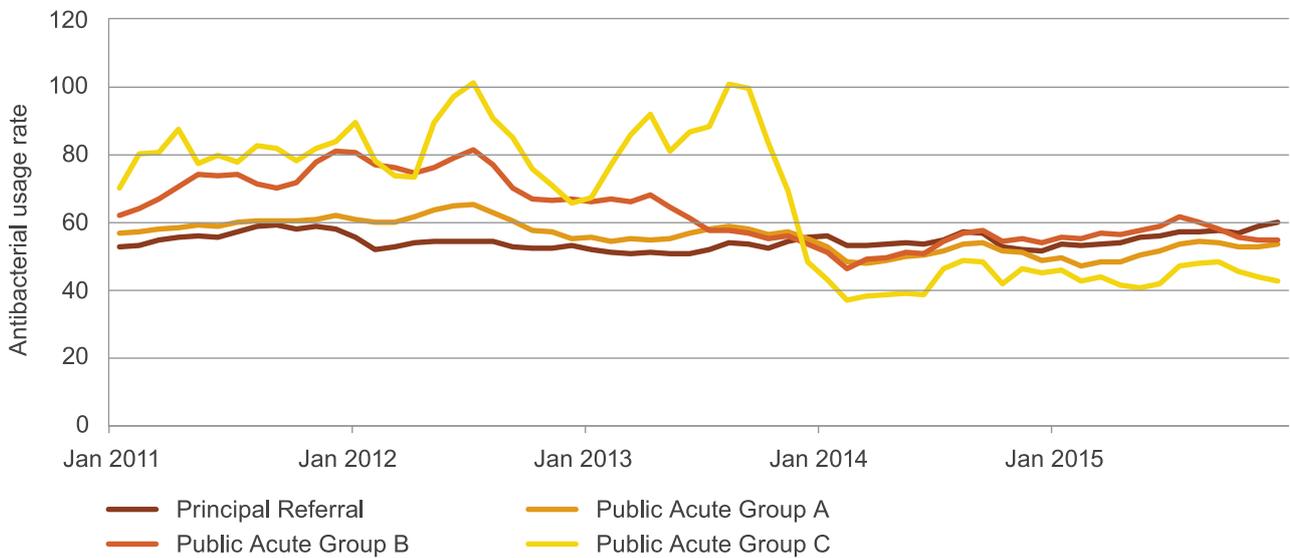
Macrolide usage rates show seasonal variation; use peaks in the winter months (Figure 3.11). Differences in use between hospital peer groups are not as pronounced for macrolides as for other antibacterial classes. Most NAUSP contributor hospitals do not have restrictions on macrolides, except for intravenous azithromycin.

Figure 3.8: Aminoglycoside usage rates (DDD/1,000 OBD) in NAUSP contributor hospitals, by selected peer groups, 2011-2015 (3-month moving average)



Source: NAUSP²⁰

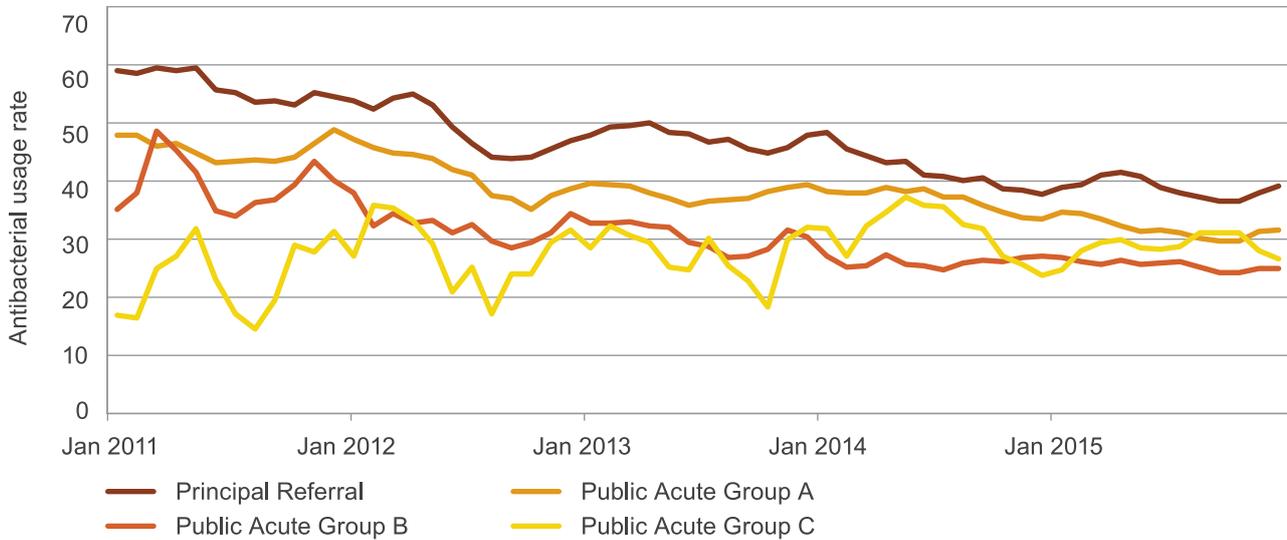
Figure 3.9: Third- and fourth-generation cephalosporin usage rates (DDD/1,000 OBD) in NAUSP contributor hospitals, by selected peer groups, 2011-2015 (3-month moving average)



Note: The drop in usage rates in November 2013 in Public Acute Group C Hospitals occurred because a hospital with very low usage rates of third- and fourth-generation cephalosporins started contributing to NAUSP in November 2013; the low numbers in this peer group caused a marked effect on the average usage rate.

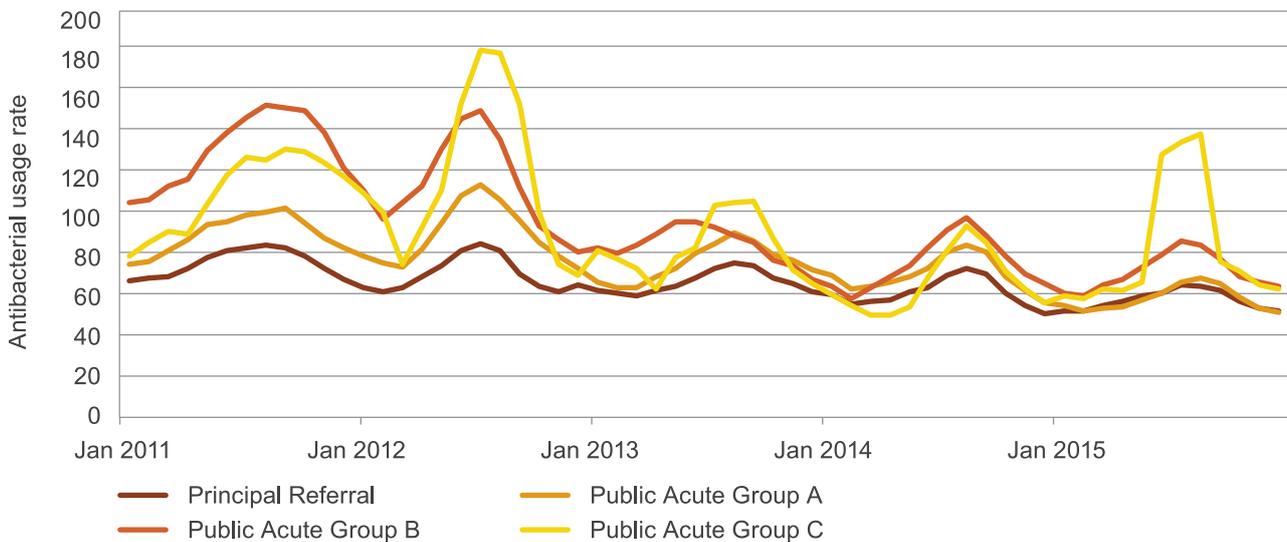
Source: NAUSP²⁰

Figure 3.10: Fluoroquinolone usage rates (DDD/1,000 OBD) in NAUSP contributor hospitals, by selected peer groups, 2011-2015 (3-month moving average)



Source: NAUSP²⁰

Figure 3.11: Macrolide usage rates (DDD/1,000 OBD) in NAUSP contributor hospitals, by selected peer groups, 2011-2015 (3-month moving average)



Source: NAUSP²⁰

Most hospital peer groups showed a decline in the use of aminoglycosides, third- and fourth-generation cephalosporins, fluoroquinolones, and macrolides.

Use of highly reserved antibacterials is mostly confined to Principal Referral and Public Acute Group A Hospitals that contributed to NAUSP from 2011 to 2015. These antibacterials are used to treat people who are seriously ill when the causative organisms are resistant to standard treatment.

Closer analysis of use of restricted antibacterials by Principal Referral Hospitals shows variation in usage rates. The average usage rate of colistin in this peer group for 2015 was 1.13 DDDs per 1,000 OBDs. The median was 0.3 DDDs per 1,000 OBDs (range 0–7.78 DDDs per 1,000 OBDs). Similarly, for daptomycin and linezolid, although average usage rates were low (1.86 and 1.59 DDDs per 1,000 OBDs, respectively), the annual rates in the hospitals with highest use were more than quadruple the average rate. Aggregate use of these restricted antibacterials in NAUSP contributor hospitals increased in the second quarter of 2015.

Appropriateness of prescribing in hospitals

In total, 22,021 prescriptions were included in NAPS 2015 for 14,389 people. In 2013, there were 12,800 prescriptions for 7,700 people; in 2014, there were 19,944 prescriptions for 12,634 people. Because of methodological requirements for the 2015 survey, only hospitals that conducted whole-hospital audits – point prevalence surveys (PPS), serial point prevalence surveys (sPPS) or a randomised sample – were included in these analyses. Most hospitals conducted a whole-hospital PPS, followed by an sPPS or a randomised sample. A small number of hospitals used the previous period prevalence survey (PePS) survey methodology because their surveys were conducted before the 2015 Hospital NAPS was launched. Since PePS was used in previous surveys, results for these hospitals were included in the analyses of 2015 Hospital NAPS data.

The prevalence of AU (that is, the percentage of hospital inpatients receiving an antimicrobial on the Hospital NAPS audit day) was 40.5%, based on data submitted from hospitals that conducted a PPS, an sPPS (only data from the first audit day were used) or a randomised sample. This is similar to that reported in the literature (21.4–54.7%).²² There was no difference in prevalence across hospital types.

On the day of the Hospital NAPS survey, 40.5% of people in hospital received at least one antimicrobial.

In hospitals, 23.3% of the 22,021 prescriptions did not comply with guidelines, and 21.9% were inappropriate. Of surgical prophylaxis prescriptions, 27.4% were continued beyond 24 hours (less than 5% is considered best practice). These findings are an improvement on those reported in the 2013 and 2014 surveys (41.8% and 35.9%, respectively; Table 3.3). However, it is unclear whether this is because of changes in the characteristics of participating hospitals or real improvement across all hospitals. A more detailed breakdown of these results by state and territory, peer group, remoteness and funding type is presented in *AURA 2017: Supplementary data*.

In hospitals, 23.3% of prescriptions did not comply with guidelines, and 21.9% were inappropriate.

The six most commonly prescribed antibacterials in the 2015 Hospital NAPS were cefazolin (13.6%), ceftriaxone (9.0%), metronidazole (6.5%), piperacillin–tazobactam (6.3%), amoxicillin–clavulanate (6.3%) and cefalexin (5.0%).

The quality of prescribing of cephalosporins was particularly poor, with 39.2% of cefalexin prescriptions, 27.3% of cefazolin prescriptions and 29.5% of ceftriaxone prescriptions found to be inappropriate (Figure 3.12). Most cefazolin prescriptions were for surgical prophylaxis (82.2%). Higher levels of appropriateness were seen for narrower-spectrum antibacterials, including trimethoprim–sulfamethoxazole, benzylpenicillin and flucloxacillin, than for broad-spectrum antimicrobials.

Table 3.3: Results for key Hospital NAPS indicators, 2013–2015

Key indicator	Percentage of total prescriptions			Percentage change from 2014 to 2015		
	2013	2014	2015	Absolute change*	Relative change†	
Indication documented in medical notes (best practice >95%)	70.9	74.0	72.5	-1.5	-2.0	
Review or stop date documented (best practice >95%)	na	na	35.5	na	na	
Surgical prophylaxis given for >24 hours (best practice <5%)§	41.8	35.9	27.4	-8.5	-24.0	
Compliance with guidelines	Compliant with <i>Therapeutic Guidelines: Antibiotic</i> or local guidelines#	59.7 (72.2)	56.2 (73.7)	55.9 (70.6)	-0.3	-1.0
	Noncompliant#	23.0 (27.8)	24.3 (26.3)	23.3 (29.4)	-1.0	-4.0
	Directed therapy	na	10.4	12.4	2.0	19.0
	No guideline available	11.0	4.6	3.8	-0.8	-17.0
	Not assessable	6.3	4.5	4.7	0.2	4.0
Appropriateness	Appropriate (optimal and adequate)**	70.8 (75.6)	72.3 (75.9)	73.2 (77.0)	0.9	1.0
	Inappropriate (suboptimal and inadequate)**	22.9 (24.4)	23.0 (24.1)	21.9 (23.0)	-1.1	-5.0
	Not assessable	6.3	4.7	5.0	0.3	6.0

na = not applicable

* Figures represent the change between 2014 and 2015 (2015 percentage minus 2014 percentage).

† Figures represent the percentage change between 2014 and 2015 expressed as a percentage of the 2014 base year.

§ Where surgical prophylaxis was selected as the indication (3,404 prescriptions in 2015).

Figures in brackets refer to prescriptions for which compliance was assessable (17,429 prescriptions in 2015). The denominator excludes antimicrobial prescriptions marked as 'directed therapy', 'not available' or 'not assessable'.

** Figures in brackets refer to prescriptions for which appropriateness was assessable (20,929 prescriptions in 2015). The denominator excludes antimicrobial prescriptions marked as 'not assessable'.

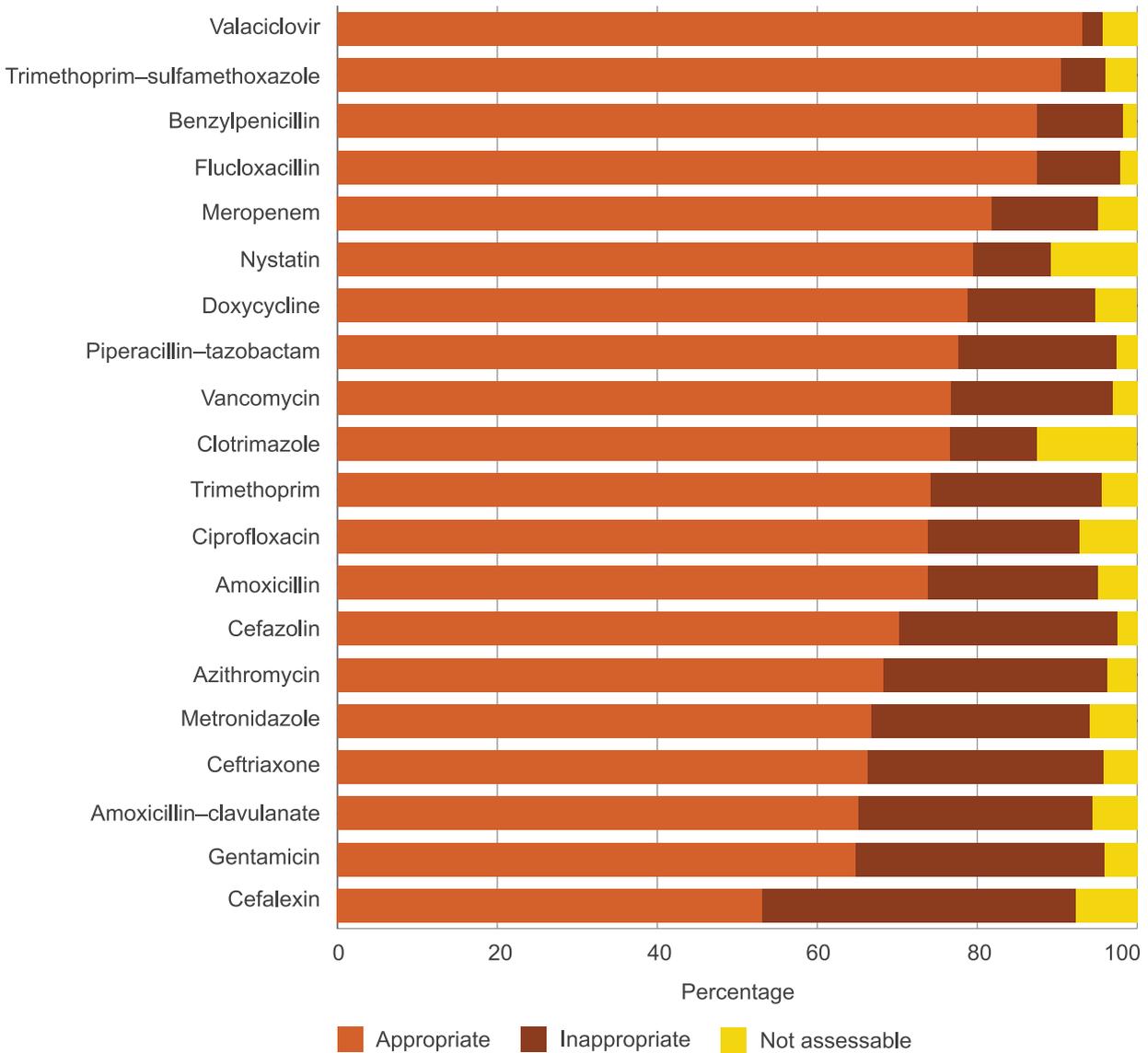
Source: Hospital NAPS²²

Higher levels of appropriateness were seen for narrower-spectrum antibacterials, including trimethoprim–sulfamethoxazole, benzylpenicillin and flucloxacillin, than for broad-spectrum antimicrobials.

Appropriateness of indications

The five most common indications were similar to those reported in AURA 2016 (Figure 3.13). The proportion of surgical prophylaxis prescriptions has slightly increased; this may be because more private hospitals are participating in the 2015 Hospital NAPS than in previous years, and private hospitals are more likely to perform a higher volume of surgical procedures than public hospitals.³¹

Figure 3.12: Appropriateness of prescribing for the 20 most commonly prescribed antimicrobials in hospitals, 2015

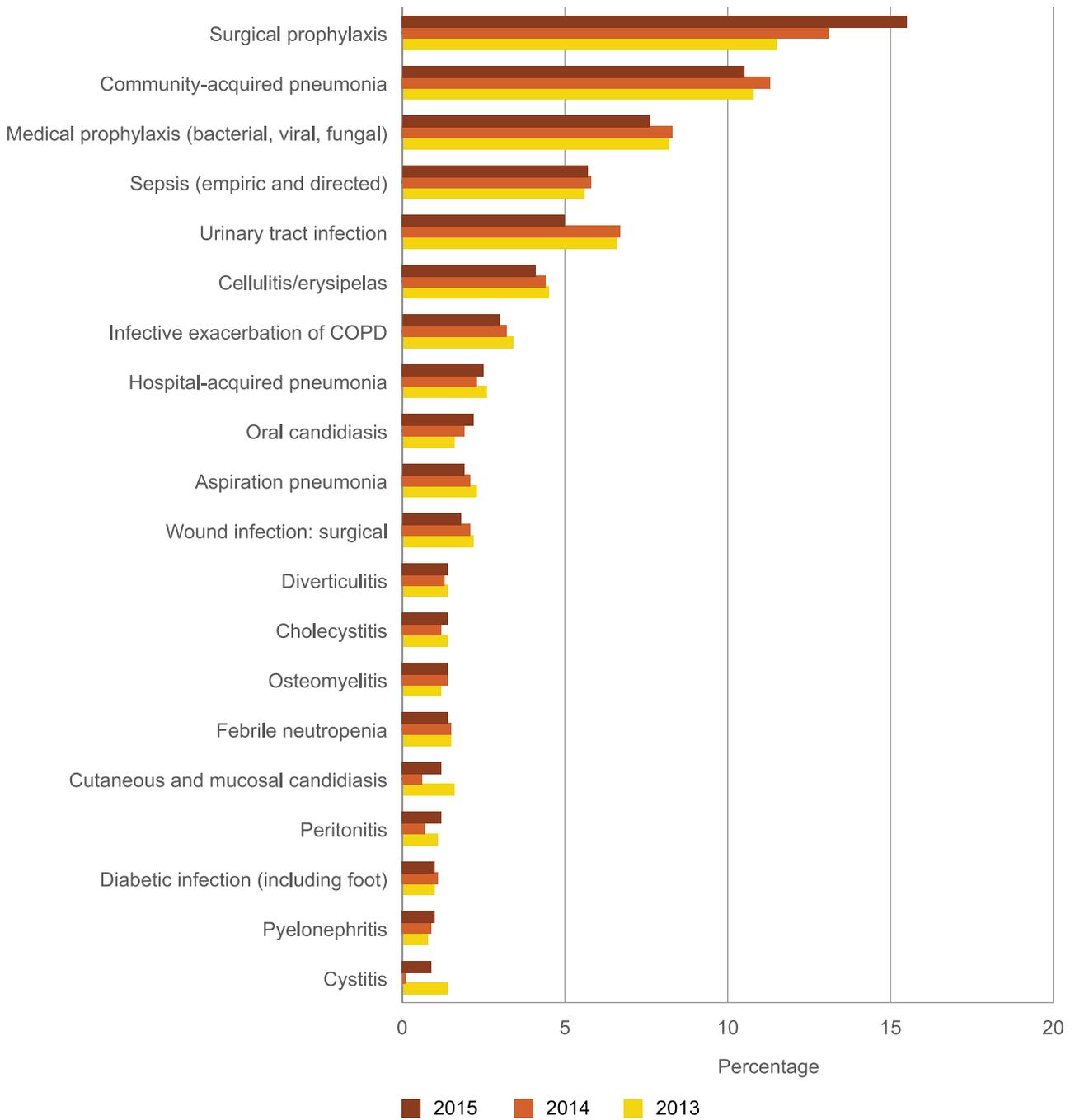


Source: Hospital NAPS²²

In public hospitals, community-acquired pneumonia (9.4%), medical prophylaxis (6.9%) and surgical prophylaxis (6.4%) were the most common indications for prescribing. In private hospitals, surgical prophylaxis was the most common indication (9.1%), followed by urinary tract infection (1.1%) and community-acquired pneumonia (1.1%). In hospitals where

data were collected in a suitable format for benchmarking, about 1 in 5 (21.9%) prescriptions was inappropriate. Of these, 53.8% were suboptimal and 46.2% were inadequate. See *AURA 2017: Supplementary data* for levels of appropriateness of prescribing for the 20 most common indications.

Figure 3.13: The 20 most common indications for prescribing in public and private hospitals, 2013–2015



COPD = chronic obstructive pulmonary disease
 Source: Hospital NAPS²²

● From information to action

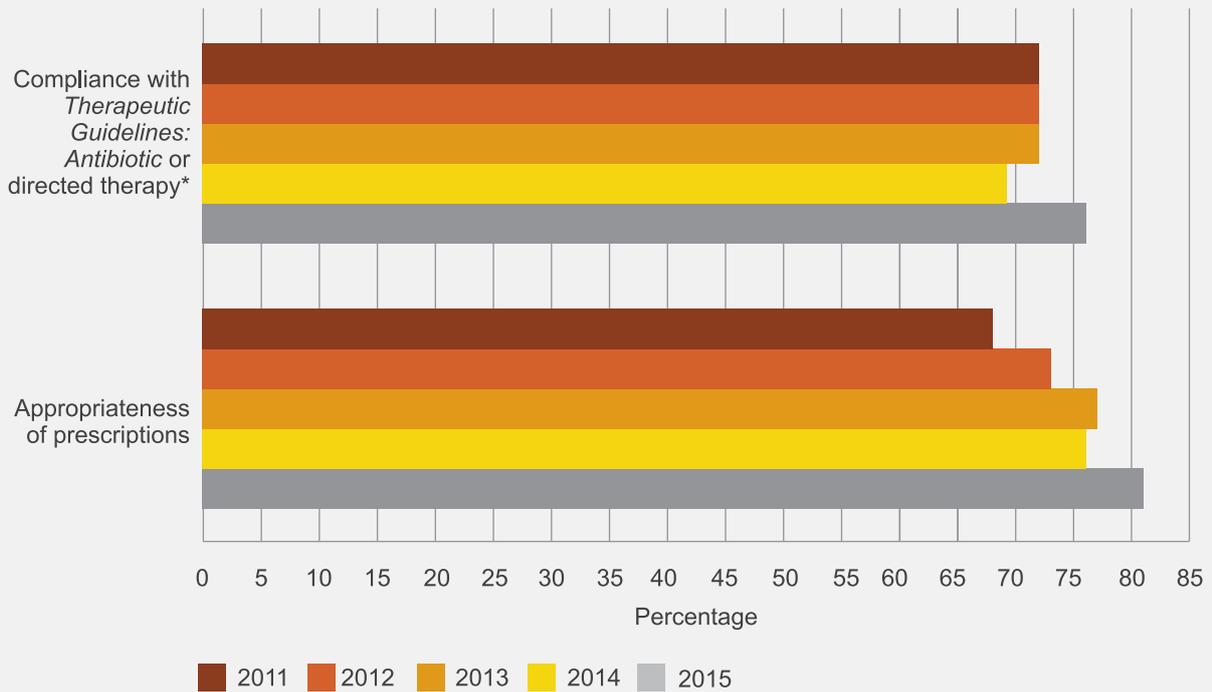
Improving appropriateness of prescribing in a large metropolitan hospital

A tertiary metropolitan hospital in New South Wales has been participating in the National Antimicrobial Prescribing Survey (NAPS) since 2011 as part of its antimicrobial stewardship (AMS) program. The 550-bed teaching hospital has a dedicated AMS pharmacist and support from infectious diseases physicians. A formal AMS program has been in place since 2012. AMS activities include antimicrobial restriction, audit

and feedback, prescriber education, daily AMS rounds, and an electronic decision-support and approval system. Guidelines and restrictions have been developed and are updated in collaboration with colleagues across the Local Health District.

The hospital participates in NAPS every year. The use of guidelines and the appropriateness of antimicrobial prescribing have steadily improved over the past five years, and this improvement has been attributed to the AMS program (Figure A).

Figure A: Appropriateness of prescribing at a New South Wales metropolitan hospital, 2011–2015



* In 2014, NAPS created a new category under 'compliant with guidelines' to capture patients on directed therapy. This was assessed as 'compliant', so both categories are included in this figure.

continued

● From information to action: continued

The hospital uses NAPS data to evaluate antimicrobial prescribing, and provides this evaluation to the hospital executive and individual units. Unit data are extracted from the NAPS database and benchmarked against other large hospitals. In 2014 and 2015, NAPS data were shared digitally across the hospital using a dynamic interface (Microsoft Sway) to inform prescribing and encourage improvements. The AMS pharmacist and infectious diseases physician who run the AMS program also met with individual units to highlight their individual results and discuss specific areas for improvement, such as management of community-acquired pneumonia.

NAPS is a useful tool to evaluate antimicrobial prescribing in this hospital, particularly the ability to benchmark antimicrobial prescribing at both the hospital and unit level against hospitals of similar size or patient casemix. Combined with other AMS interventions and evaluation, this yearly audit and data have contributed to consistent improvements in antimicrobial prescribing at the hospital.

Surgical prophylaxis remains an area for focused strategies to improve prescribing practice. A total of 40.5% of these prescriptions were assessed as inappropriate, mainly because of incorrect duration (29.9%), incorrect dose (27.6%) and the procedure not requiring antimicrobial prophylaxis (22.0%). For more information on surgical prophylaxis, see Section 3.3.

High rates of inappropriateness of prescribing were seen for several respiratory tract infections. Rates of inappropriateness for infective

exacerbation of chronic obstructive pulmonary disease (COPD) were similar to those in 2014 (34.3% in 2015 and 36.8% in 2014), as were the rates of inappropriateness for community-acquired pneumonia (24.4% in 2015 and 25.0% in 2014). Rates of inappropriate prescribing decreased for bronchitis and exacerbations of asthma compared with 2014, but the numbers were small. The most common reasons for inappropriate prescribing for these three conditions were that the spectrum was too broad (49.8%) and the indication did not require an antibacterial (15.5%).

Of all inappropriate prescriptions, the three most common reasons for inappropriate prescribing were that the spectrum was too broad, the indication did not require an antibacterial and the dose was incorrect.

Conditions with high levels of inappropriate prescribing were similar to those that did not comply with guidelines. See *AURA 2017: Supplementary data* for details of compliance with guidelines for the 20 most common indications. Overall, 23.3% of prescriptions did not comply with guidelines. This includes situations where, for example, the antimicrobial chosen was appropriate, but the dose or frequency did not comply with guidelines. The two most common reasons for not complying with guidelines were that the spectrum was too broad (26.4%), and dose or frequency was incorrect (22.0%). Indications with high levels of not complying with guidelines were similar to those with high levels of inappropriateness, such as surgical prophylaxis, infective exacerbation of COPD and cholecystitis.

The three most common reasons for inappropriate prescribing were that the spectrum was too broad, the indication did not require an antibacterial and the dose was incorrect.

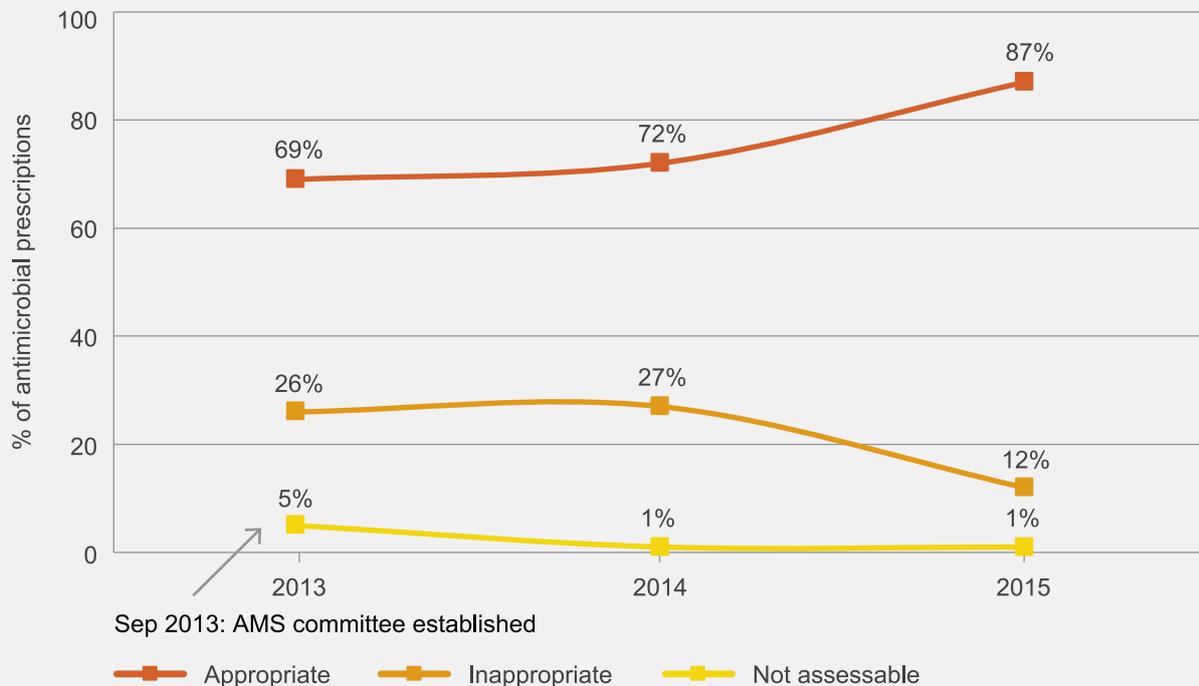
● From information to action

Demonstrating the effects of antimicrobial stewardship interventions

A large metropolitan hospital in South Australia uses the National Antimicrobial Prescribing Survey (NAPS) as a core surveillance tool to support its antimicrobial stewardship (AMS) program. This hospital is the major acute care hospital for the health region and offers a broad range of clinical services. An AMS committee oversees the AMS program across the region, and infectious diseases physicians are on site. The hospital does not have a dedicated AMS pharmacist, although clinical and dispensary pharmacists play key roles in AMS, including maintaining the formulary restriction process.

The hospital has performed a whole-of-hospital (admitted patients) NAPS survey each year since 2013. Results are presented to the entire hospital during Antibiotic Awareness Week, and relevant results are also communicated directly to specific units. The number of patients audited has steadily increased each year, from 231 patients in 2013 to 298 patients in 2015, corresponding to the growth in acute care services offered at the hospital. The percentage of patients receiving antimicrobials during 2013–2015 has remained consistent (both locally and nationally) at around 38%.

Figure A: Antimicrobial prescribing in a large metropolitan hospital, 2013–2015



Source: NAPS data from the hospital, 2013–2015

continued

● From information to action: continued

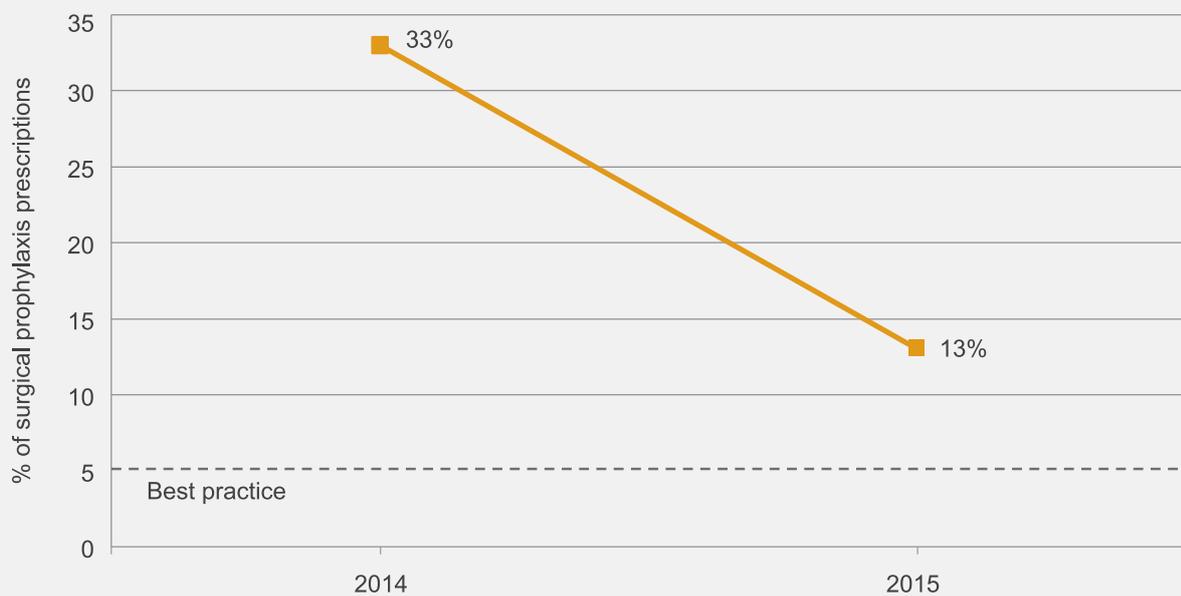
Conducting the NAPS every year has been a very useful tool for the hospital – it has allowed the hospital to track AMS progress over time and to see the effect of specific interventions. Appropriateness of antimicrobial prescribing has increased sharply over the three years of NAPS involvement (Figure A). This coincides with the initiation of the AMS program in 2013 and continuing development of the program since then.

In 2014, a key area of focus for AMS was to reduce the number of antimicrobial prescriptions for surgical prophylaxis that continued for more than 24 hours. The NAPS

results for surgical prophylaxis were also communicated to clinicians. Figure B shows the improvement in surgical prophylaxis prescribing in the following year.

In 2015, a key issue identified was the appropriateness of antimicrobials prescribed for chronic obstructive pulmonary disease (COPD) – 86% of these prescriptions were deemed inappropriate. The hospital initiated education and awareness initiatives, and prescriber feedback to address this issue. This approach was so successful that, in a post-intervention audit, all COPD prescriptions were deemed appropriate.

Figure B: Surgical prophylaxis prescribed for >24 hours, 2014–15



Source: NAPS data from the hospital, 2014–15

Commentary

Overall antimicrobial use

Australia's AU has gradually declined since its peak in 2010. In 2011, total AU was 992.4 DDDs per 1,000 OBDs; in 2015, it was 916 DDDs per 1,000 OBDs – a reduction of 7.6 percentage points.

Factors that are likely to have contributed to reduced use include:

- Increased capacity of local, state and territory, and national AMS programs
- Changes in clinical practice and more effective adoption of recommendations in *Therapeutic Guidelines: Antibiotic*²³
- Variation in World Health Organization-defined DDDs and the doses currently used in clinical practice (although, in most cases, variations led to falsely increased usage rates).

AURA 2017: Supplementary data includes data on changes in usage rates for antimicrobial classes between 2014 and 2015. Notable changes were seen for the following antibacterial classes (the changes are shown in brackets):

- Aminoglycosides (-15.9%)
- Extended-spectrum penicillins (-10.3%)
- Fluoroquinolones (-9.7%)
- Macrolides (-9.4%)
- Tetracyclines (+18.6%)
- β -lactamase-sensitive penicillins (+14.2%).

There was a notable decrease in the use of broader-spectrum or more toxic agents, accompanied by an increase in the use of narrow-spectrum β -lactams). One reason for the decrease in aminoglycoside use could be that prescribers stop aminoglycoside therapy after 48–72 hours if culture results do not support their ongoing use, as recommended in *Therapeutic Guidelines: Antibiotic* since 2014.²³

Variation in antimicrobial use

There is large variation in the rate of AU between states and territories, and both within and

between hospital peer groups. Some variation is expected because of factors such as casemix and local resistance patterns. Understanding variation improves the appropriateness of prescribing, but there are not enough data to identify which factors are driving variation in volume of AU and prescribing in hospitals. This would be a useful area of review to optimise clinical and prescribing practice.

Understanding variation improves the appropriateness of prescribing, but there are not enough data to identify which factors are driving variation in volume of antimicrobial use and prescribing in Australian hospitals.

Consumption of broader-spectrum and reserve-line antimicrobials is higher in settings with a more complex patient mix; usage rates across most classes are 2–3 times higher in Principal Referral Hospitals than in smaller hospitals, as shown in the 2015 NAUSP report. However, Principal Referral Hospitals had the lowest usage rates of third- and fourth-generation cephalosporins, and macrolides. This may reflect variations in prescribing, local susceptibility patterns, and the effect of local, or state or territory AMS programs.

Twenty antibacterials accounted for 93% of use on a DDD basis. Six antibacterials – amoxicillin–clavulanate, cefazolin, amoxicillin, flucloxacillin, doxycycline and cefalexin – represented 54% of antibacterials supplied in NAUSP contributor hospitals. In 2014, these six were also the most commonly used antibacterials and accounted for 51% of antibacterials supplied in NAUSP contributor hospitals.

Among antibacterial classes, β -lactamase inhibitor combinations had the highest rate of use, followed by first-generation cephalosporins,

extended-spectrum penicillins, β -lactamase-resistant penicillins, tetracyclines and macrolides.

Macrolides show the most seasonal variation in usage rates, peaking in the winter months. Azithromycin is the main macrolide used. The interstate variation in macrolide usage rates may be related to different prescribing patterns for respiratory tract infections (for example, community-acquired pneumonia).

Appropriateness of prescribing

Data from the 2015 Hospital NAPS show between 53.1% and 93.1% appropriateness of prescribing for the 20 most commonly used antimicrobials. Cephalosporins were the most commonly prescribed class in the 2015 Hospital NAPS, accounting for more than 25% of prescribing: cefazolin (13.6%), ceftriaxone (9.0%) and cefalexin (5.0%). The appropriateness

● From information to action

Using NAPS and NAUSP data to revise restriction protocols

In one Principal Referral Hospital in eastern Australia that does not have a semi-automated electronic approvals system, the antimicrobial stewardship (AMS) team investigated alternative strategies for reducing the hospital's use of broad-spectrum antimicrobial agents, especially ceftriaxone and piperacillin-tazobactam.

To inform changes to the local antimicrobial prescribing policy that would improve appropriateness of prescribing, the AMS team analysed the hospital's local data on the duration of prescriptions, as well as its data on appropriateness from the National Antimicrobial Prescribing Survey (NAPS). During the local analysis of the NAPS data, the AMS team also gave consideration to the availability of AMS staff to review restricted antimicrobial prescriptions and the limited availability of decision support tools.

The analysis showed that 60–66% of ceftriaxone and piperacillin-tazobactam use was for longer than three days (that is, beyond 72 hours). This accounted for 108 days of excess broad-spectrum therapy for ceftriaxone and 114 days for piperacillin-tazobactam. Shorter duration therapy (that is, less than 72 hours) accounted for significantly fewer days

of excess therapy – 76 days for ceftriaxone and 42 days for piperacillin-tazobactam.

In view of these findings, the AMS team revised the restriction points for ceftriaxone and piperacillin-tazobactam (and other 'orange' antimicrobials throughout the hospital) to midday on day three of therapy, rather than at 24 hours. This change created an opportunity to switch from intravenous to oral antimicrobials, and ensure appropriate oral and 'step-down' antimicrobial therapy choice, often supported by radiology and microbiology results that may have become available. Clinicians continued to exercise clinical autonomy for appropriate antimicrobial prescribing within the first three days, resulting in improved clinician acceptance of the revised restriction procedure.

Six months after implementation, NAPS data showed a relative 24% increase in prescribing appropriateness (14% absolute increase). Nine months after implementation, data from the National Antimicrobial Utilisation Surveillance Program showed an absolute reduction of 20% on average in total-hospital antimicrobial usage across oral and intravenous therapies. Use of some antimicrobial classes decreased by 40% or more (Table A).

continued

● From information to action: continued

Table A: Changes in antimicrobial use nine months after implementing the revised restriction procedure

Antibiotic class	Absolute change in use in 2016 compared with 2015 (%)
Trimethoprim and derivatives	-56
Amoxicillin-clavulanate	-40
Fluoroquinolones	-40
Lincosamides	-38
Glycopeptides	-36
Trimethoprim-sulfamethoxazole	-31
First-generation cephalosporins	-27
Nitroimidazoles	-25
Macrolides	-25
β -lactamase-sensitive penicillins	-22
Piperacillin-tazobactam	-21
Extended-spectrum penicillins	-20
Carbapenems	-15
β -lactamase-resistant penicillins	-12
Tetracyclines	+9

of prescribing of oral cefalexin – the sixth most commonly prescribed antibacterial – is a particular concern, because about 40% of these prescriptions were inappropriate.

Overall, 21.9% of prescriptions in the 2015 Hospital NAPS were inappropriate. The most common reasons for inappropriate prescribing were that the spectrum was too broad, the indication did not require an antibacterial and the incorrect dose was prescribed. Inappropriate prescribing was very common for some respiratory infections – in particular, infective exacerbation of COPD, infective exacerbation of asthma, and bronchitis. Surgical prophylaxis and infective exacerbation of COPD were the conditions for which prescribing most often did not comply with guidelines.

Gaps and improvements

Strengthening NAUSP

The Australian Commission on Safety and Quality in Health Care (the Commission) has worked with SA Health to strengthen the system for NAUSP. The changes included creation of a web portal, which was activated in May 2016, to streamline data entry and processing for contributing hospitals, and make it easier for them to generate reports as required on their total-hospital and intensive care unit antibacterial use. To assist with benchmarking, contributing hospitals can also access state- or territory-level usage reports, which are updated quarterly.

● From information to action

Strengthening antimicrobial stewardship

Antimicrobial surveillance programs were implemented in two public acute hospitals within a rural New South Wales Local Health District (LHD) in early 2013. These programs included contributing data to the National Antimicrobial Utilisation Surveillance Program (NAUSP), conducting the annual point prevalence National Antimicrobial Prescribing Survey (NAPS) and using a paper-based restriction process at one hospital.

Both hospitals contributed data to the 2013 and 2014 NAUSP and NAPS. Analysis of these data revealed that they were not sufficiently robust to provide a foundation for quality improvement. For example, 52.5% of the NAPS prescriptions in 2013 were deemed 'not assessable', and data were being interpreted incorrectly. Data were not provided as feedback to prescribers at either hospital, and compliance with the paper-based restriction process was only 10%.

In 2015, these results contributed to a decision to appoint an antimicrobial stewardship (AMS) pharmacist and an infectious diseases specialist across the network, and to implement an electronic AMS program in both hospitals.

The AMS team reviewed NAUSP data and compliance with the electronic AMS program. The review identified antimicrobial overuse and misuse, particularly the use of ceftriaxone for surgical and respiratory admissions.

In response, the AMS team implemented an education program for prescribers, and restriction protocols to target the use of ceftriaxone. For example, the AMS team declined any inappropriate prescriptions for ceftriaxone that were submitted using the

electronic AMS program and reported the reasons for declining to the treating team. This process provided valuable immediate feedback and information to guide changes in prescribing practice, and resulted in a sustained decrease in ceftriaxone use (Figure A).

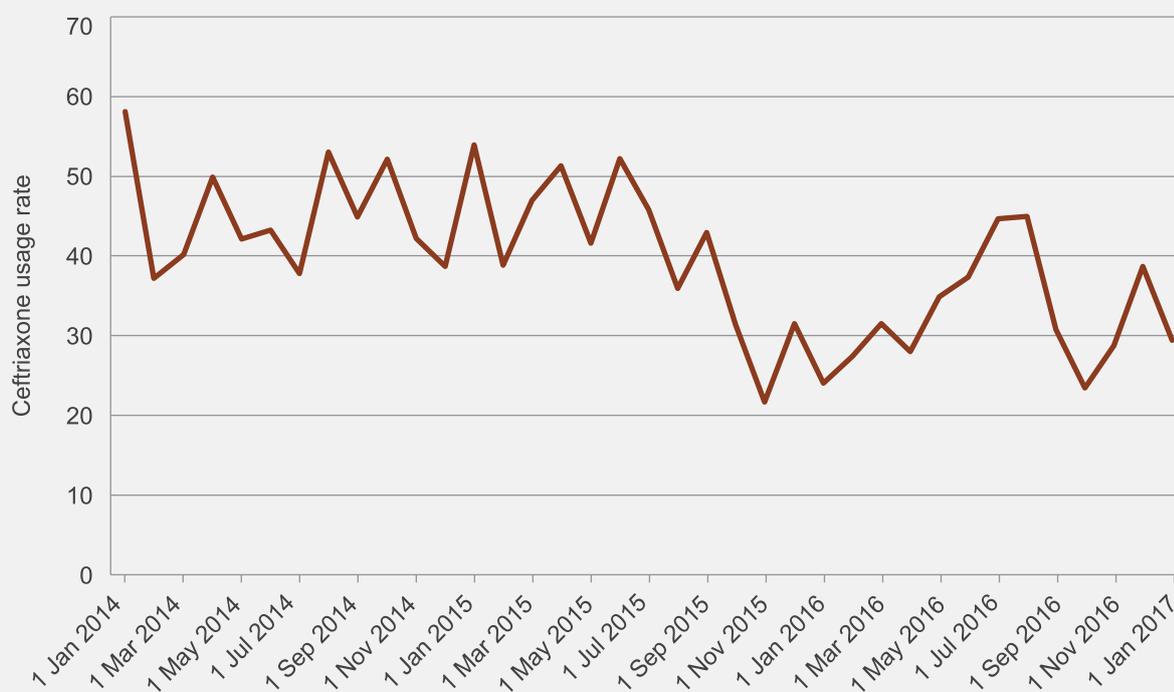
The use of hospital antibiograms also helped to reduce inappropriate ceftriaxone prescribing. The antibiogram allowed prescribers to clearly see that ceftriaxone had inferior coverage to the therapies recommended in national guidelines, particularly for urinary tract pathogens. The appropriateness of ceftriaxone prescribing has improved, and the percentage of ceftriaxone prescriptions that were inappropriate decreased by 6.1% between 2015 and 2016.

After the first year of intervention, the number of patients in the Hospital in the Home program who required management by the AMS team was reduced by 29.1%. Prescribing of ceftriaxone for cellulitis in Hospital in the Home patients, which was identified through peripheral site surveillance, has ceased completely.

Since 2015, there has been a positive shift in attitudes towards, and increased involvement in, AMS activities within the LHD. Establishing an antimicrobial restriction program is considered to have been a key driver for behaviour change. The changes have also resulted in buy-in from nursing specialties, medical practitioners, pathology services and pharmacy services, because communication between these groups has increased as part of the AMS program and antimicrobial treatment plans.

continued

● From information to action: continued

Figure A: Ceftriaxone usage rate (DDD/1,000 OBD) at a hospital in rural New South Wales, 2014–2017

Source: NAUSP data, 2014–2017

3.2 Antimicrobial use in the community – primary care

AMR is found more frequently, and the intensity of AU is much greater, in hospitals. However, most AU occurs in the community setting (general practice, specialist outpatients, dental clinics and aged care homes). This section includes data on AU in the community; analyses of AU stratified by age, antimicrobial class and prescriber type; variation in AU across Australia; and appropriateness of AU. Data on use in primary care primarily relate to antibacterial use.

Antimicrobial use in aged care homes represents a particular challenge and is addressed in Section 3.3.

Antimicrobial use in primary care

The volume of AU is derived from the Australian Government Department of Human Services pharmacy claim records of prescriptions dispensed under the Pharmaceutical Benefits Scheme (PBS) and the Repatriation Pharmaceutical Benefits Scheme (RPBS), and the Drug Utilisation Sub Committee database.³² Data are from the 2015 calendar year. Data include dispensing data on antimicrobials prescribed by general practitioners, specialists and approved non-medical prescribers in the community, as well as prescriptions written in public hospitals for outpatients and patients on discharge from hospital, and for inpatients of private hospitals. There are some small differences in the ATC classifications used by the Drug Utilisation

Sub Committee database and the PBS/RPBS, resulting in a variance in total prescription numbers of around 3%.

Information on variation in prescribing across local areas, and states and territories, and according to socioeconomic status, was obtained from two sources: the *Australian Atlas of Healthcare Variation*³³ and the MedicinesInsight program.* MedicinesInsight data were also used to identify the usage patterns of seven antimicrobials commonly used in general practice, and to assess appropriateness of prescribing against recommended treatments in *Therapeutic Guidelines: Antibiotic*²³ and quality indicators developed by the European Surveillance of Antimicrobial Consumption Network (ESAC-Net).†

Volume of antimicrobial use

In 2015, around half (44.7%; $n = 10,701,804$) of the Australian population had at least one antimicrobial dispensed under the PBS/RPBS. Of these, 18.5% had one antimicrobial dispensed, and 3.2% had more than six antimicrobial prescriptions dispensed, including repeats. These figures are very similar to the 2014 data reported in AURA 2016.⁶

The supply of PBS/RPBS systemic antimicrobials in 2015 totalled 27,667,198 prescriptions, which equated to 25.4 DDDs per 1,000 inhabitants per

day, or 1,163 prescriptions per 1,000 inhabitants (Figure 3.14). This was a 6.7% increase in DDDs per 1,000 inhabitants per day compared with 2014. A further 2,785,173 prescriptions were supplied for non-systemic (topical) preparations, making a total of 30,452,371 prescriptions (1,280 prescriptions per 1,000 inhabitants) for antimicrobials.

Figure 3.15 shows the distribution of classes of systemic antimicrobials dispensed in 2015. Extended-spectrum penicillins represent the largest group by number of prescriptions dispensed in 2015 (21% of prescriptions), followed by first-generation cephalosporins (20%) and penicillin-β-lactamase inhibitor combinations (18%). This is consistent with data reported in AURA 2016. Australia places heavy reliance on broad-spectrum β-lactams, which have more potential to select for resistance to multiple drug classes.

The 11 most commonly dispensed antimicrobials accounted for 84% of all AU in 2015 (Table 3.4). This is consistent with data reported in AURA 2016.

Figure 3.16 presents the quarterly number of prescriptions dispensed for six agents: four with prominent seasonal variation (amoxicillin, amoxicillin-clavulanate, roxithromycin and doxycycline), and two with no seasonal variation (cefalexin and trimethoprim). The four with seasonal variation are the agents most commonly dispensed for the treatment of respiratory tract infections. Cefalexin is most commonly used for skin and soft tissue infections, and trimethoprim is used exclusively for the treatment and prevention of lower urinary tract infections.

Averaging the data for one year (four-quarter rolling average – Figure 3.17) shows the trends for the 10 most commonly dispensed systemic antibacterial agents. In the past 20 years, there have been substantial increases in the consumption of cefalexin, amoxicillin-clavulanate, clarithromycin and trimethoprim.

* MedicinesInsight is an NPS MedicineWise program in which around 500 general practices from across Australia participate. More than 2,000 general practitioners, representing more than 2 million patients contributed to the program in 2015. Real-time data are collected regularly, analysed and reported back to practices to provide insight into a range of clinical indicators, including antimicrobial prescribing.

† ESAC-Net (formerly ESAC) is a Europe-wide network of national surveillance systems, providing European reference data on antimicrobial consumption. ESAC-Net collects and analyses data on antimicrobial consumption from European Union and European Economic Area/ European Free Trade Association countries, both in the community and in the hospital sector.

The increase in cefalexin consumption was initially driven by a nationally distributed warning about the potential hepatotoxicity of flucloxacillin in the early 1990s, but use of cefalexin has continued to rise even as flucloxacillin use has risen again from its lowest level in 2003.

Trimethoprim has slowly supplanted the trimethoprim-sulfamethoxazole combination for the treatment and prevention of urinary tract infection. Substantial decreases have occurred in the consumption of cefaclor and erythromycin. It is likely that use of cefaclor has fallen because of its rate of adverse drug reactions in children, and the availability of other agents with paediatric formulations for the treatment of respiratory tract infections. Erythromycin use has decreased as a result of increasing availability of other macrolides that are better tolerated (roxithromycin) or targeted at respiratory tract infection (for example, clarithromycin, which was first marketed in 1998).

In 1998, public hospital pharmaceutical reforms were introduced that allow public hospitals to supply outpatient and discharge prescriptions under the PBS. This may have influenced the trends of AU to a small extent. In 2013, public hospital pharmacies accounted for 1% of antimicrobial prescriptions supplied, and private hospital pharmacies a further 1%.³⁴

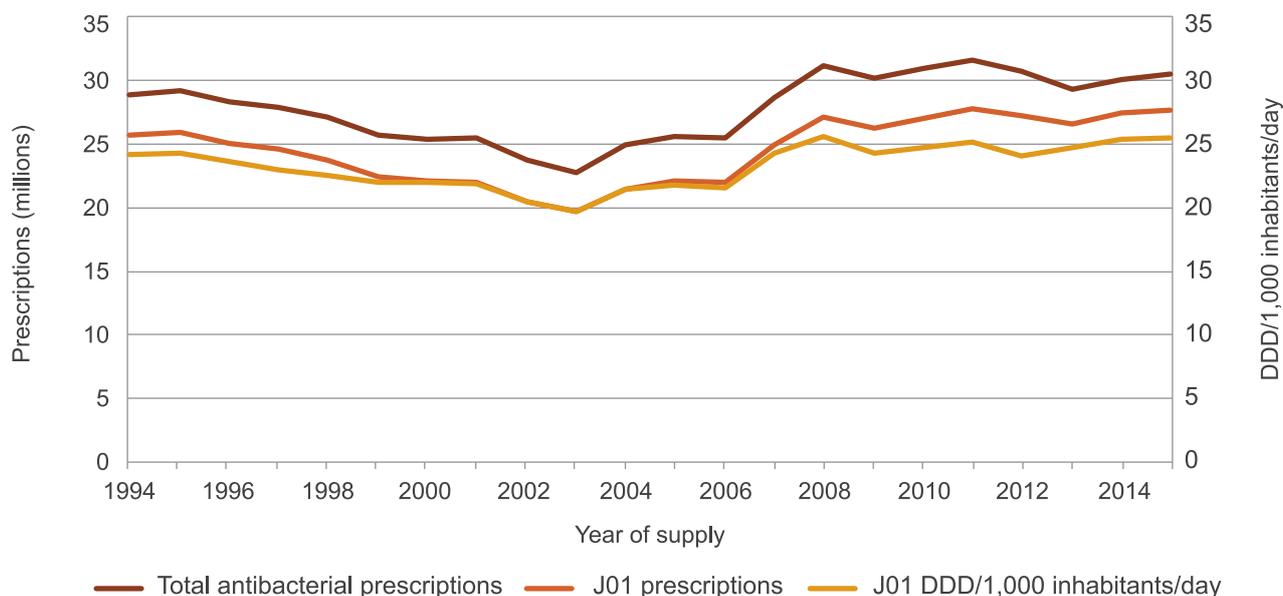
Use by age

Antimicrobials were most often dispensed in community settings for very young people and older people. In 2015, 51% of those aged 0–4 years, 60% of those aged 65 years or over, and 76% of those aged 85 years or over were supplied at least one antimicrobial (Figure 3.18). These proportions have been generally consistent for several years, although the proportion of prescriptions dispensed for the 0–4-year age group in 2015 (51%) was lower than that reported in 2014 (57%). AU in all age groups is higher during the winter months.

Antimicrobials were most often dispensed in community settings for very young people and older people.

Figure 3.19 presents data on dispensing for the four most frequently used therapeutic groups by age group. Twice the proportion of children aged 0–9 years were dispensed extended-spectrum penicillins than other age groups, whereas the proportion of patients older than 65 years dispensed a first-generation cephalosporin was two to three times the proportion dispensed to younger patients. A similar pattern of prescribing was seen for macrolides and penicillin- β -lactamase inhibitor combinations, with a higher proportion of prescriptions dispensed for patients older than 65 years than for younger patients. Individual figures for the 11 most commonly dispensed antimicrobials by age group are provided in *AURA 2017: Supplementary data*.

Figure 3.14: Number of antimicrobials dispensed under the PBS/RPBS, 1994–2015



Notes:

1. J01 is the ATC code for antibacterials for systemic use.
2. Data relating to the number of prescriptions dispensed before April 2012 include estimates of under co-payment and private dispensing. Data relating to the number of prescriptions dispensed after April 2012 include actual under co-payment data, but no estimate for private dispensing. The data on DDD/1,000 inhabitants/day exclude some items for which there is no DDD.

Source: Drug Utilisation Sub Committee database, 2017

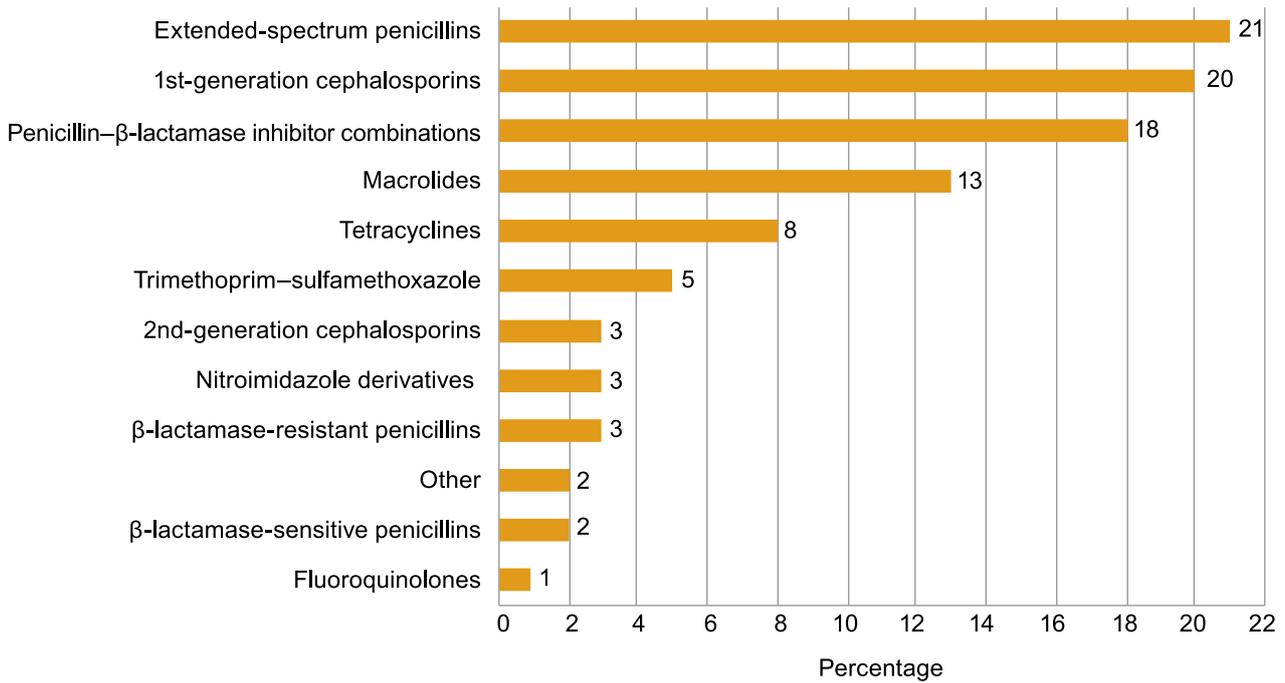
Table 3.4: The 11 most commonly dispensed antimicrobials under the PBS/RPBS, by number of prescriptions dispensed and percentage change, 2014–15

Antimicrobial	Number of prescriptions dispensed in 2014	Number of prescriptions dispensed in 2014 per 1,000 inhabitants	Number of prescriptions dispensed in 2015	Number of prescriptions dispensed in 2015 per 1,000 inhabitants	Absolute % change, 2014 to 2015
Amoxicillin	5,870,123	248	5,864,658	244	-1.6
Cefalexin	5,549,606	234	5,604,590	234	0.0
Amoxicillin-clavulanate	4,897,449	207	5,067,228	211	1.9
Doxycycline	1,900,200	80	2,022,676	84	4.8
Roxithromycin	1,851,821	78	1,774,312	74	-5.4
Chloramphenicol	1,167,191	49	1,263,895	52	5.8
Clarithromycin	949,562	40	1,007,353	42	4.8
Trimethoprim	920,857	38	923,288	38	0.0
Erythromycin	841,350	35	824,879	34	-2.9
Flucloxacillin	694,076	29	723,177	30	3.3
Cefaclor	636,619	26	564,001	23	-13.0

Note: Includes actual under co-payment data, but no estimate for private dispensing.

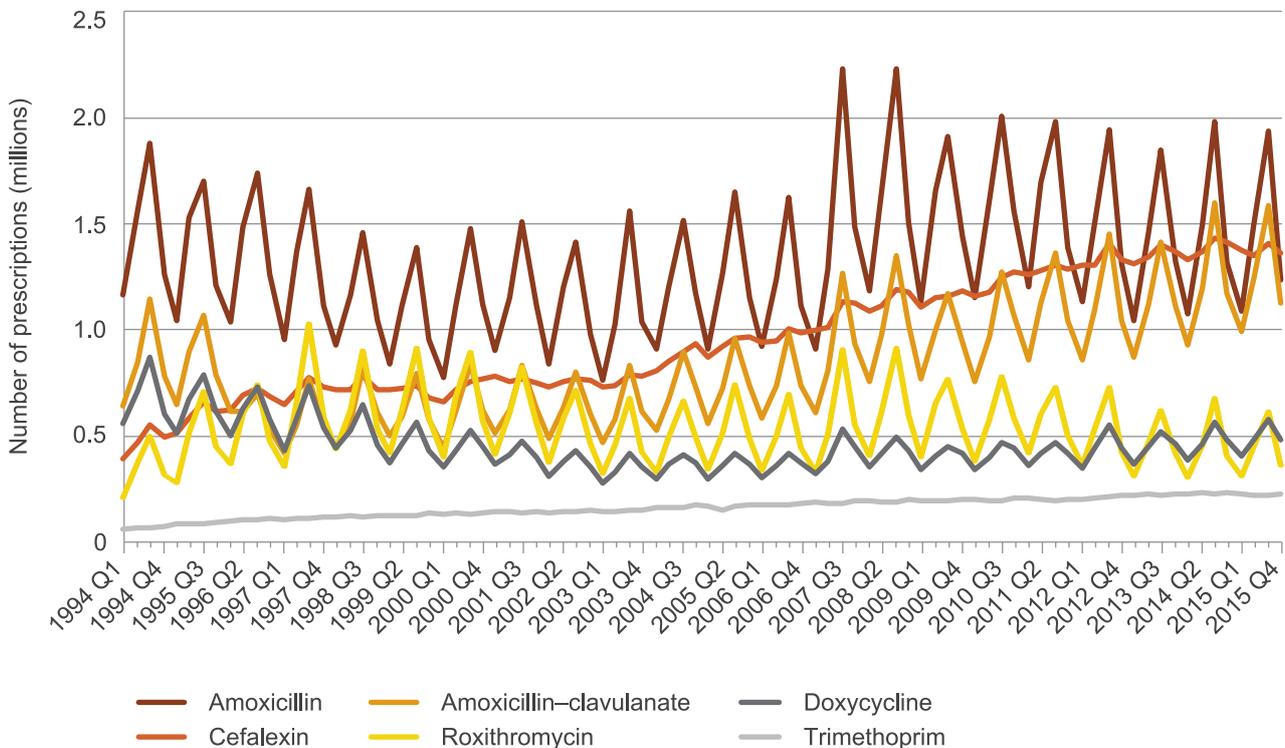
Source: Drug Utilisation Sub Committee database, February 2017

Figure 3.15: Systemic antimicrobial dispensing, by class, 2015



Note: Includes actual under co-payment data, but no estimate for private dispensing.
 Source: Department of Human Services pharmacy claims database, 2015

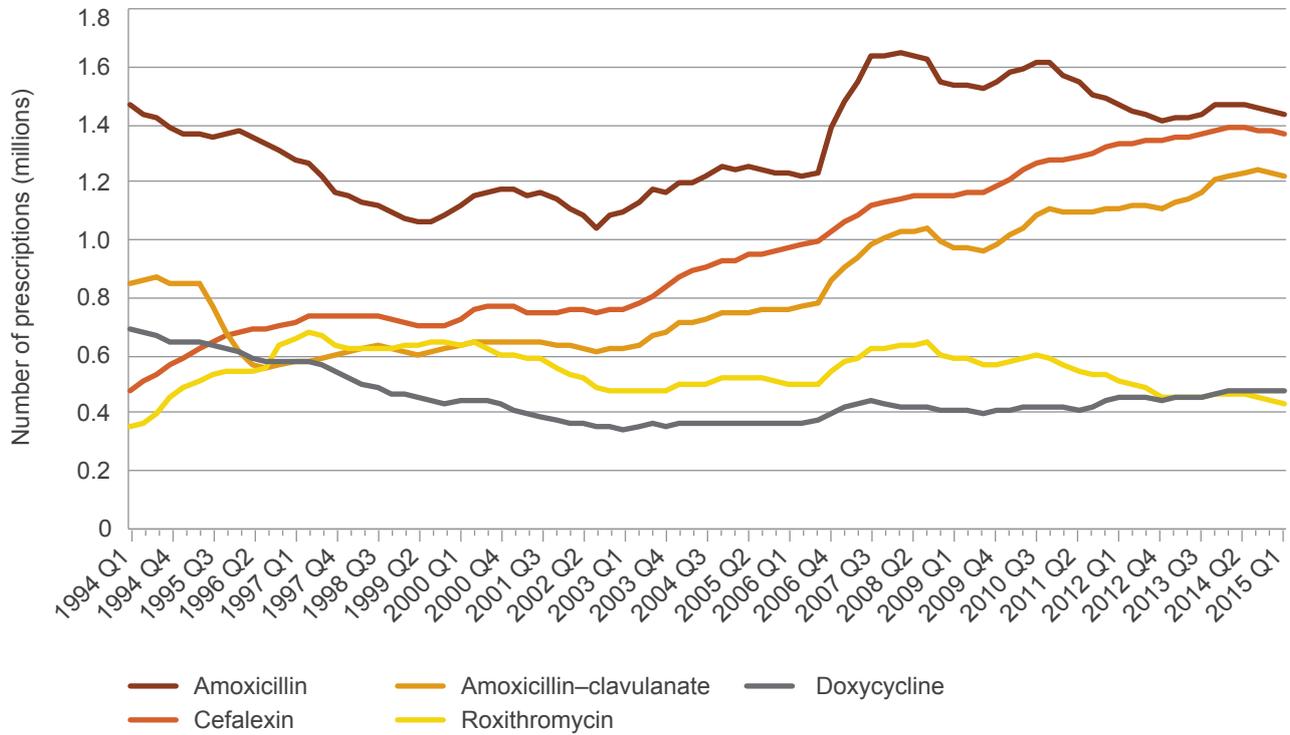
Figure 3.16: The six most commonly dispensed antimicrobials under the PBS/RPBS, by number of prescriptions and by quarter, 1994–2015



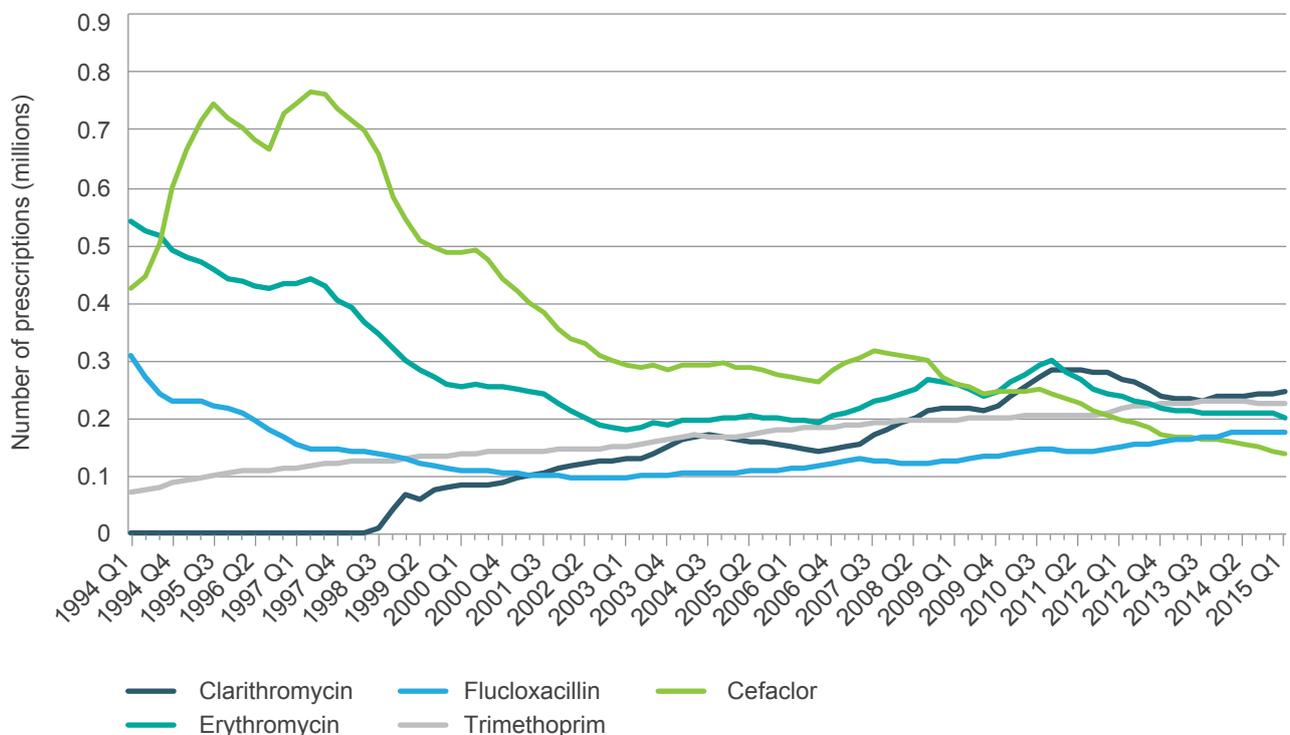
Note: Before April 2012, includes estimates of under co-payment and private dispensing; after April 2012, includes actual under co-payment data, but no estimate for private dispensing.
 Source: Drug Utilisation Sub Committee database to the end of 2014; Department of Human Services pharmacy claim database data for 2015

Figure 3.17: The 10 most commonly dispensed antimicrobials under the PBS/RPBS, by number of prescriptions and by quarter (four-quarter moving average), 1994–2015

Amoxicillin, cefalexin, amoxicillin–clavulanate, roxithromycin and doxycycline



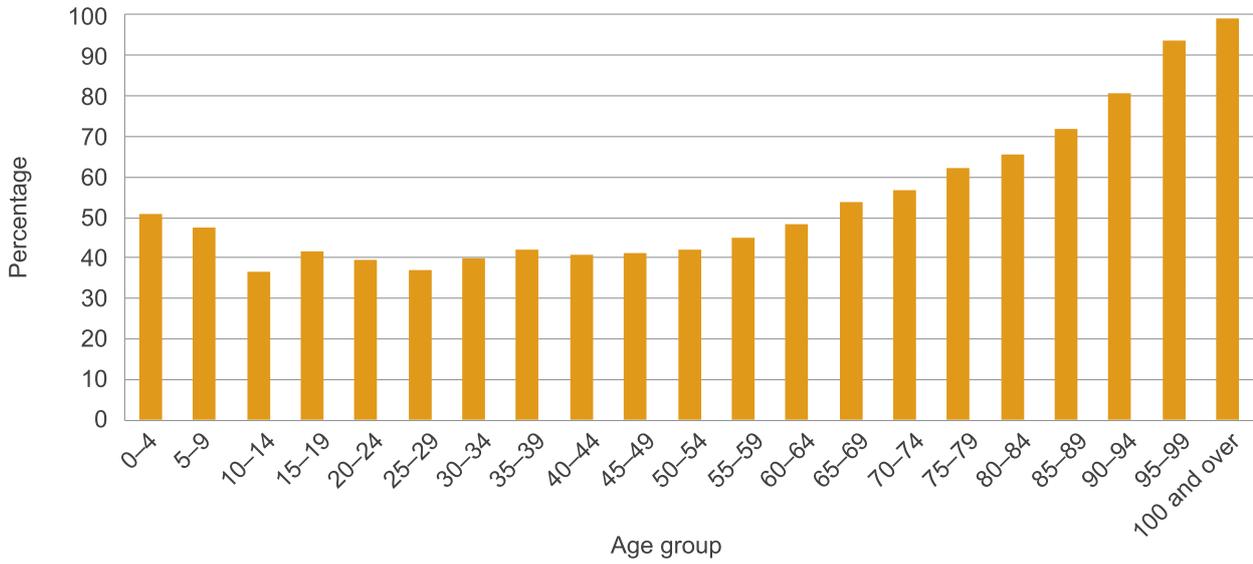
Clarithromycin, erythromycin, flucloxacillin, trimethoprim and cefaclor



Note: Data relating to the number of prescriptions dispensed before April 2012 include estimates of under co-payment and private dispensing. Data relating to the number of prescriptions dispensed after April 2012 include actual under co-payment data, but no estimate for private dispensing.

Source: Drug Utilisation Sub Committee database to the end of 2014; Department of Human Services pharmacy claim database data for 2015

Figure 3.18: Percentage of the population supplied at least one antimicrobial under the PBS/RPBS, by age group, 2015



Notes:

1. Data are age standardised based on the estimated resident population by age at 30 June 2015.⁵⁵
2. Includes actual under co-payment data, but no estimate for private dispensing.

Source: Department of Human Services pharmacy claim database, January 2017

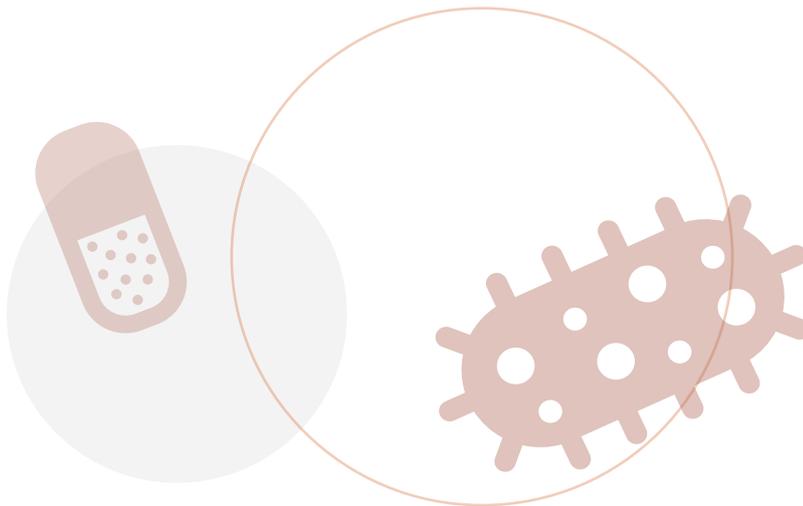
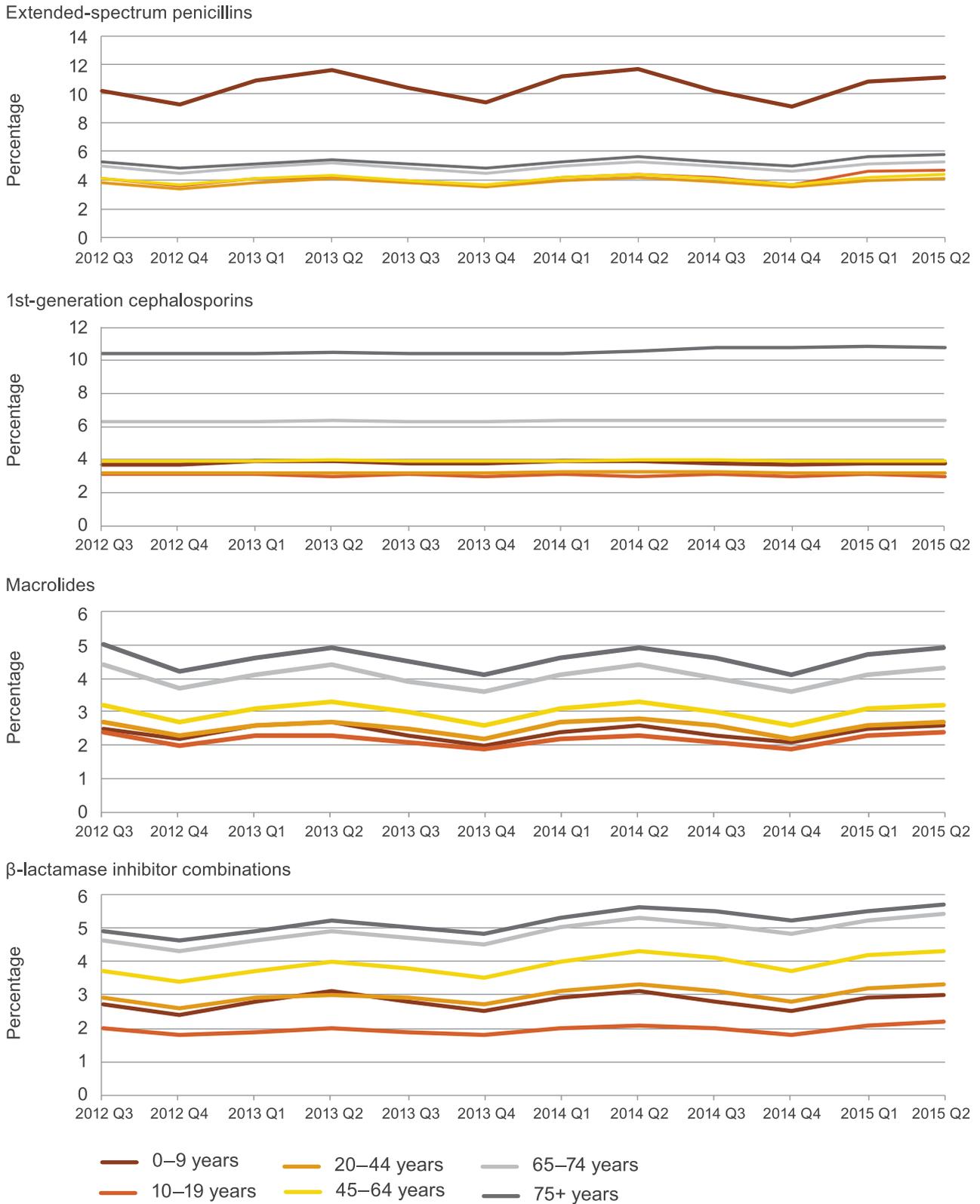


Figure 3.19: Percentage of the population supplied any PBS/RPBS antimicrobial, by age group (three-point moving average), 2012–2015



Notes:

1. Data are age standardised based on the estimated quarterly resident population by age.³⁵
2. Includes actual under co-payment data, but no estimate for private dispensing.

Source: Department of Human Services pharmacy claims database, January 2017

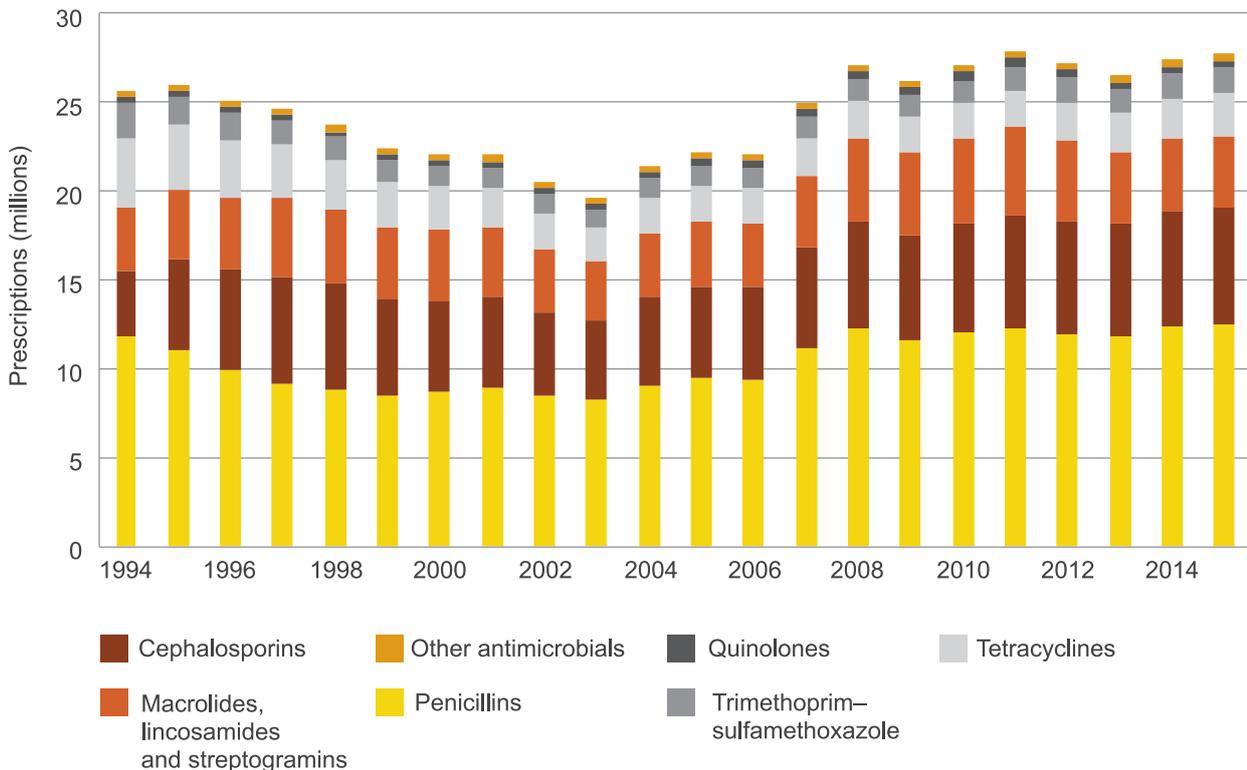
Use by therapeutic group

The relative contribution of each antimicrobial group to AU has not changed markedly during the past 20 years (Figure 3.20). The use of cephalosporins has been slowly expanding, with an increase in cefalexin more than compensating for the diminished used of cefaclor (Figure 3.20). Changes within the class to broader-spectrum agents (for example, amoxicillin to amoxicillin-clavulanate) are likely to have a greater effect on resistance selection than changes between classes. Penicillins continue to be the largest contributor to overall use (45% in 2015, compared with 44% in 2014).

Of the penicillin and cephalosporin prescriptions dispensed in 2015, narrow-spectrum agents accounted for 8% of AU, moderate-spectrum agents for 65% of AU and broad-spectrum agents for 27% of AU.

Chloramphenicol eye preparations dominate the supply of ophthalmic and otic antimicrobials, although combination corticosteroid and anti-infective ear drops also contribute a large proportion (Figure 3.21). Note that chloramphenicol eye drops and eye ointment have been available without a prescription as pharmacist-only supply since May 2010³⁶; this supply is not included in the analysis and therefore underestimates its use.

Figure 3.20: Number of systemic PBS/RPBS antimicrobial prescriptions dispensed, by therapeutic group, 1994–2015



Notes:

1. 'Other antimicrobials' include amphenicols and aminoglycosides.
2. Includes under co-payment estimate and actual, and includes private estimate.

Source: Gadzhanova and Roughead³²

Appropriateness of prescribing in primary care

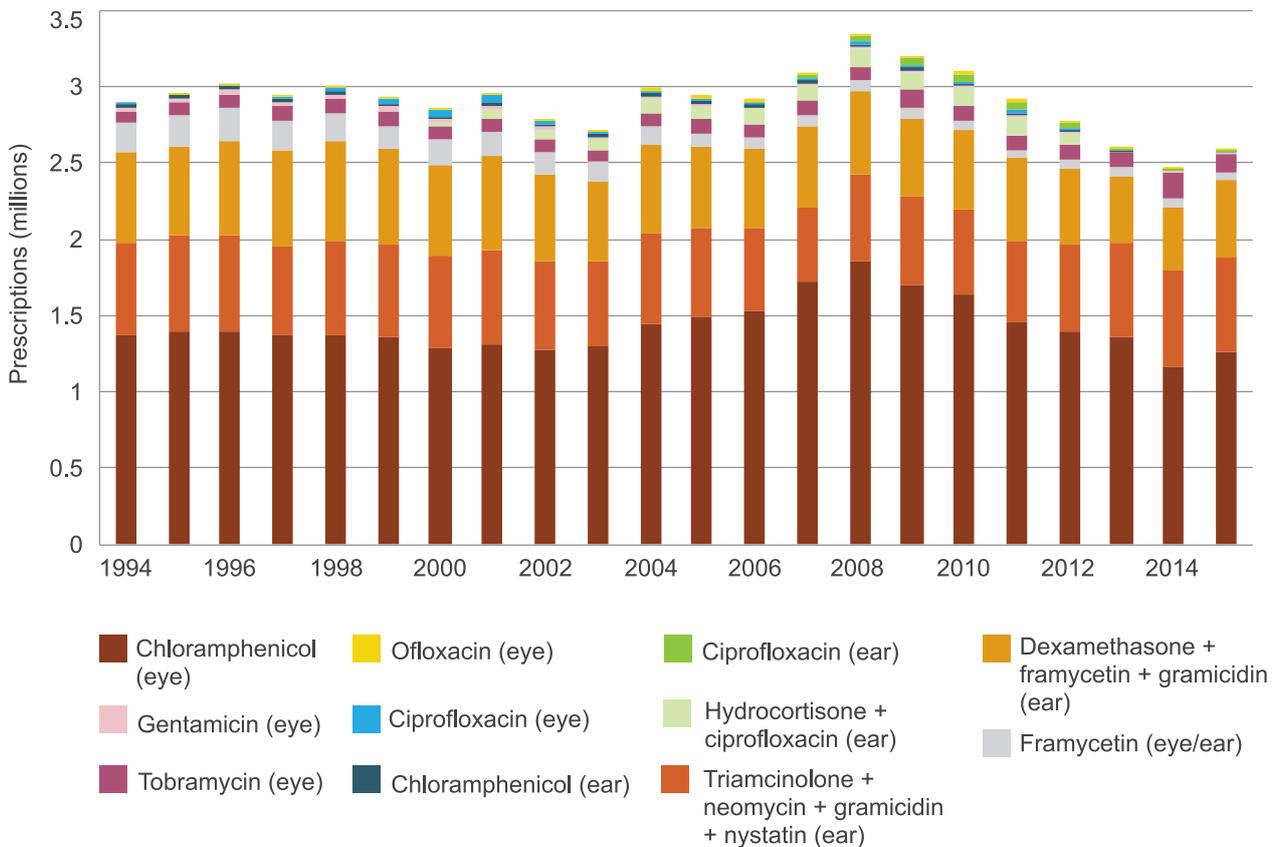
The MedicineInsight program provides information on patterns of systemic AU, as well as the demographic characteristics and risk factors of patients prescribed systemic antimicrobials. It also assesses the appropriateness of prescribing for specific conditions such as upper respiratory tract infections and urinary tract infections.

Thirty per cent of MedicineInsight patients (968,259 out of 3,181,923) were prescribed systemic antimicrobials between 1 January and 31 December 2015.³⁷ Females and older people were more likely to receive a prescription. New

South Wales had higher prescribing rates (31.1 per 100 patients) than other states (24.5–31.0 per 100 patients), and people living in major cities had higher rates of systemic antimicrobials prescribed than residents of other regions. People living in the most disadvantaged Socio-Economic Indexes for Areas decile had the highest rates of antimicrobial prescribing (32.1%), although not substantially higher than the overall rate. *AURA 2017: Supplementary data* has more information on this topic.

The rate of antimicrobial prescriptions (originals) per 100 general practitioner consultations has shown a small decline from 2010 to 2015, and shows an expected pattern of seasonal variation (Figure 3.22), driven by winter respiratory tract

Figure 3.21: Number of ophthalmic and otic antimicrobial preparations dispensed under the PBS/RPBS, by therapeutic group, 1994–2015



Notes:

1. Includes under co-payment estimate and actual, and includes private estimate
2. Chloramphenicol eye drops and eye ointment have been available without a prescription as pharmacist-only supply since May 2010; this supply is not included in the analysis.

Source: Gadzhanova and Roughead³²

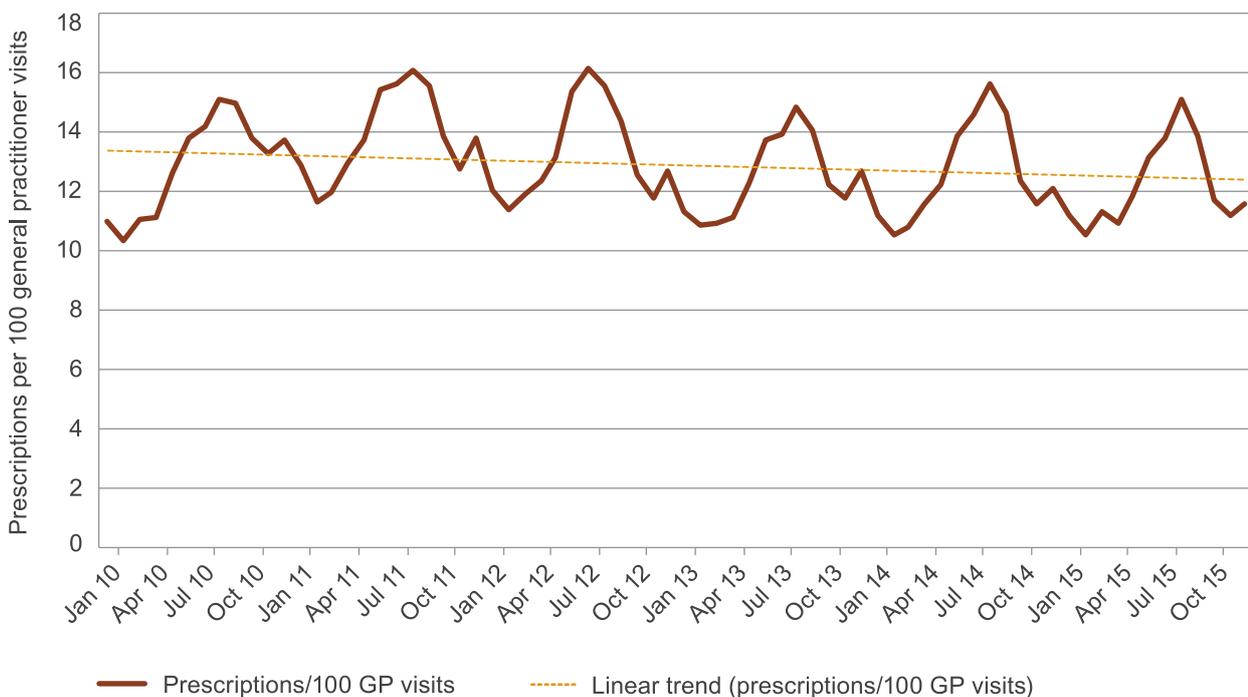
infections. This pattern is similar to the variation seen in amoxicillin, amoxicillin-clavulanate, macrolide and doxycycline prescriptions, with peaks in winter and troughs in summer.

Only 23.5% of patients prescribed antimicrobials in 2015 had an indication recorded for the prescription in their health record. This low rate may in part be due to some information being documented in progress notes that MedicineInsight does not collect. Of these people, 60% who were reported to have colds and other upper respiratory tract infections were prescribed an antimicrobial – antimicrobials are not generally recommended for these conditions. A large proportion of patients with more specifically documented types of upper respiratory tract infections (such as acute tonsillitis, acute or chronic sinusitis, acute otitis media or acute bronchitis) were reported to have been prescribed an antimicrobial, despite guidelines recommending that antimicrobials are not indicated as routine therapy for these

conditions (Table 3.5). A large proportion of the antimicrobials prescribed were not consistent with the first recommendation in Australian guidelines.²³ Concordance with guidelines varied from 27% for sinusitis to 67% for pneumonia. For some conditions, the antimicrobial prescribing rate was 3.0–4.5 times as high as that recommended by ESAC-Net. Only prescriptions of antimicrobials for urinary tract infections or cystitis met the ESAC-Net acceptable range for prescribing (Table 3.5).

In AURA 2016, MedicineInsight data were reported for 2014 from 183 participating general practices. In AURA 2017, data are reported from more than 423 general practices. Some of the differences in results can be attributed to the significant expansion of the program and the characteristics of participating practices.

Figure 3.22: Rate of general practitioner PBS/RPBS prescriptions for systemic antimicrobials (originals only) per 100 visits, January 2010 to December 2015



Source: NPS MedicineWise³⁷

Table 3.5: Number and percentage of patients prescribed systemic antimicrobials by general practitioners for selected conditions, confidence intervals and acceptable range, 2015

Condition	Patient	2015			Acceptable range (%)
		Number	Percentage	95% CI	
Acute URTI	Older than 1 year prescribed antibacterials*	125,291	60	58-62	0-20
Acute bronchitis or bronchiolitis	Aged 18-75 years prescribed antibacterials*	70,882	93	92-94	0-30
Acute tonsillitis	Older than 1 year prescribed antibacterials	28,687	71	69-73	0-20
	And prescribed TG-recommended penicillin V	15,772	39	37-42	80-100
Sinusitis (chronic or acute)	Older than 18 years prescribed antibacterials	48,408	91	90-92	0-20
	And prescribed TG-recommended amoxicillin	14,451	27	26-29	80-100
Acute otitis media/myringitis	Older than 2 years prescribed antibacterials	32,490	94	93-95	0-20
	And prescribed TG-recommended amoxicillin	17,835	51	50-53	80-100
Pneumonia	Aged 18-65 years prescribed antibacterials	439	90	85-94	90-100
	And prescribed TG-recommended antibiotic (for mild CAP - amoxicillin or doxycycline)	328	67	59-75	80-100
Cystitis or other UTI	Females older than 18 years prescribed antibacterials	67,375	97	97-98	80-100
	And prescribed TG-recommended trimethoprim	22,343	32	31-33	80-100

CAP = community-acquired pneumonia; CI = confidence interval; TG = *Therapeutic Guidelines: Antibiotic*; URTI = upper respiratory tract infection; UTI = urinary tract infection

* No antibacterials recommended by *Therapeutic Guidelines: Antibiotic*

Source: NPS MedicineWise³⁷ (data for 2015 from 423 general practices participating in MedicineInsight)

Only 24% of people prescribed an antimicrobial had an indication recorded for the prescription in their health record. Of these, 60% of people who had colds and other upper respiratory tract infections were prescribed an antimicrobial, but antimicrobials are not generally recommended for these conditions.

Patterns of use of seven antimicrobials are presented in Table 3.6, including the percentage of people prescribed each agent, the main indications for use, the incidence of repeat prescribing, and differences between PBS/RPBS and private prescriptions.

The most common indication for prescribing amoxicillin, amoxicillin-clavulanate and roxithromycin was upper respiratory tract infections (Table 3.6). Amoxicillin was also commonly prescribed for otitis media. Amoxicillin-clavulanate, roxithromycin and doxycycline accounted for a significant number of prescriptions for sinusitis, bronchitis and lower respiratory tract infections. Cefalexin was widely used for urinary tract infections, and skin or soft tissue infections, although it is not recommended as a first-line treatment for these indications in *Therapeutic Guidelines: Antibiotic*.²³ Repeats appear to be overprescribed frequently, perhaps related to default settings in practice software packages.

The use of private prescriptions was highest for azithromycin, ciprofloxacin and doxycycline, but, in many cases, this appeared to be appropriate. For example, doxycycline is often prescribed for malaria prophylaxis and acne treatment, and ciprofloxacin for travel. However, there is no explanation for the high proportion of private prescriptions for azithromycin for the treatment of upper respiratory tract infections.

The high prescribing rates for amoxicillin, amoxicillin-clavulanate and roxithromycin for upper respiratory tract infections reported by MedicineInsight accord with the data published in the annual *Report on Government Services* (ROGS).⁹ ROGS reports on the measures of appropriateness of management of upper respiratory tract infections. These measures are:

- Filled general practice prescriptions for selected antimicrobials per 1,000 inhabitants (data obtained from the PBS and the RPBS on the oral antimicrobials most commonly used to treat upper respiratory tract infections – phenoxymethylpenicillin, amoxicillin, amoxicillin-clavulanate, clarithromycin, erythromycin, roxithromycin, cefaclor, cefuroxime and doxycycline)
- Proportion of visits to general practitioners for acute upper respiratory tract infections where systemic antimicrobials are prescribed.

The national aggregate number of prescriptions per 1,000 inhabitants for oral antimicrobials most commonly used to treat upper respiratory tract infections was 305 in 2014–15, similar to 2012–13 (302), and there has been a slow downwards trend overall since 2006 (Figure 3.23). However, these antimicrobials are also prescribed for other conditions, so the rate should be interpreted with caution.

The prevalence of prescriptions for oral antimicrobials commonly used to treat upper respiratory tract infections varied across states and territories (Figure 3.24). The lower rates in Western Australia and the Northern Territory may, in part, reflect other sources of supply of antimicrobials, such as Aboriginal health services (which are not included in Figure 3.24).

Table 3.6: Patterns of use, indications for therapy, repeat prescribing, and differences between general practitioner PBS/RPBS and private prescriptions for seven antimicrobials, 2015

Antimicrobial (PBS/RPBS benefit)	Patients issued a prescription (%)*	Most common indications (%)	Patient cohort	Repeats prescribed	Differences between PBS/RPBS and private prescriptions
Amoxicillin (general benefit)	7.5	<ul style="list-style-type: none"> • URTI (29%) • Otitis media (15%) • Non-respiratory infections (minority of cases) 	<ul style="list-style-type: none"> • Highest use in children 	28% of prescriptions ordered with one or more repeats	Negligible private use (<1%)
Cefalexin (general benefit)	6.4	<ul style="list-style-type: none"> • Skin and wound infections (34%) • UTI (20%) • Respiratory infections (minority of cases) 	<ul style="list-style-type: none"> • Higher use in elderly patients • Comparatively lower use in Western Australia 	42% of prescriptions ordered with one or more repeats	Negligible private use (<1%)
Amoxicillin-clavulanate (restricted to infections resistant to amoxicillin)	4.6	<ul style="list-style-type: none"> • Sinusitis (15%) • Acute URTI (13%) • Otitis media (8%) • Skin and wound infections (8%) 	<ul style="list-style-type: none"> • Higher use in patients with COPD 	57% of prescriptions ordered with one or more repeats	Negligible private use (<1%)
Roxithromycin (general benefit)	1.9	<ul style="list-style-type: none"> • URTI (28%) • Lower respiratory tract infections (15%) • Bronchitis (12%) 	<ul style="list-style-type: none"> • Higher use in older patients, and patients with COPD or asthma • Higher use in Victoria and major cities 	55% of prescriptions ordered with repeat	Negligible private use (<1%)
Doxycycline (general benefit, restricted for some indications)	2.2	<ul style="list-style-type: none"> • PBS/RPBS use: acne (15%), sinusitis (13%) • Private use: travel (69%) 	<ul style="list-style-type: none"> • Higher use in 20-29-year-olds, 80-89-year-olds, inner regional areas, and patients with COPD 	51% of prescriptions ordered with repeat	13% private use. Private prescriptions for travel
Azithromycin (restricted benefit)	0.6	<ul style="list-style-type: none"> • PBS/RPBS use: <i>Chlamydia</i> infections (43%) • Private use: acute URTI (17%), travel (12%) 	<ul style="list-style-type: none"> • Highest use in 20-29-year-olds. Higher use in Western Australia, and in outer and remote areas 	11% of PBS/RPBS prescriptions and 17% of private prescriptions ordered with one or more repeats	42% private use

continued

Table 3.6: continued

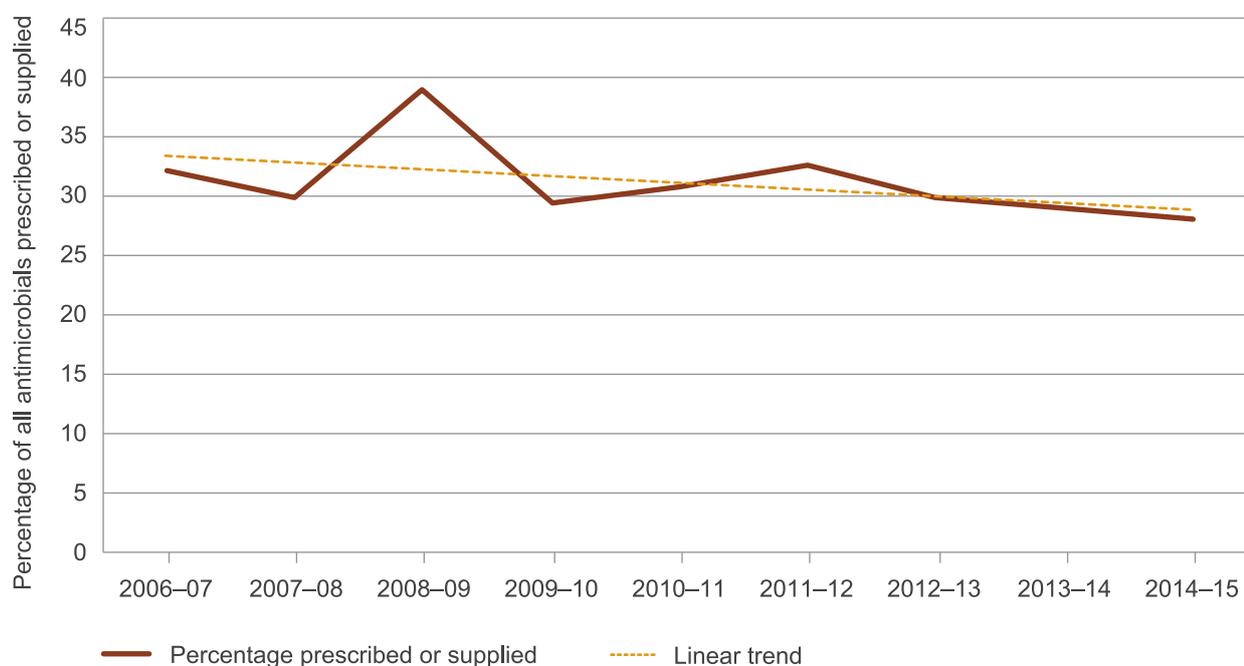
Antimicrobial (PBS/RPBS benefit)	Patients issued a prescription (%)*	Most common indications (%)	Patient cohort	Repeats prescribed	Differences between PBS/RPBS and private prescriptions
Ciprofloxacin (restricted benefit)	0.2	<ul style="list-style-type: none"> PBS/RPBS use: other infections of ear, eye, gastrointestinal tract and nail (36%); skin and wound infections (23%) Private use: travel (20%) 	<ul style="list-style-type: none"> Use increased with age; highest use in >70-year-olds and patients with COPD Lower PBS/RPBS use in Victoria and the Northern Territory 	48% of PBS/RPBS prescriptions and 13% of private prescriptions ordered with one or more repeats	27% private prescriptions. PBS/RPBS prescriptions ordered for courses of longer duration than private prescriptions

COPD = chronic obstructive pulmonary disease; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme; URTI = upper respiratory tract infection; UTI = urinary tract infection

* Percentage of patients who visited a general practitioner at least once, or had one or more prescriptions ordered in 2015 for the specified antimicrobial

Source: NPS MedicineWise³⁷ (data for 2015 from 423 general practices participating in MedicineInsight)

Figure 3.23: Proportion of general practitioner encounters for management of acute upper respiratory tract infection where systemic antimicrobials were prescribed or supplied, 2006–07 to 2014–15



Note: Prescriptions ordered by vocationally registered general practitioners and other medical practitioners, and dispensed. Data are not limited to prescriptions for the treatment of upper respiratory tract infections. Data for 2012–13 are for all people and are not comparable with data for previous years, which were limited to prescriptions provided to holders of concession cards. Data are from April to March of the following year. Participation in the survey is voluntary. Data are not necessarily representative of non-participating general practitioners. A general practitioner encounter is a professional interchange between a patient and a general practitioner. Source: ROGS, Table 10A.59⁹

Figure 3.24: Proportion of general practitioner encounters for management of acute upper respiratory tract infection where systemic antimicrobials were prescribed or supplied, by state and territory, 2006–2011 and 2010–2015



Note: Prescriptions ordered by vocationally registered general practitioners and other medical practitioners, and dispensed. Data are not limited to prescriptions for the treatment of upper respiratory tract infections. Data for 2012–13 are for all people and are not comparable with data for previous years, which were limited to prescriptions provided to holders of concession cards. Data are from April of the first year to March of the final year of each five-year period. Participation in the survey is voluntary. Data are not necessarily representative of non-participating general practitioners. A general practitioner encounter is a professional interchange between a patient and a general practitioner

Source: ROGS, Table 10A.59⁹

Commentary

Overall prescribing in the community

AU in the community setting in Australia is still very high. In 2015, 45% of the population was dispensed at least one systemic antimicrobial, with an overall rate of 25.4 DDDs per 1,000 inhabitants per day. Australia’s antimicrobial prescribing rate is the eighth highest among member countries of the Organisation for Economic Co-operation and Development, and is more than double that of countries that prescribe the lowest rate of antimicrobials.³⁸

Although PBS/RPBS data indicate that 45% of people were dispensed an antimicrobial in 2015³², MedicineInsight data indicate that 30% of patients attending a general practitioner in 2015 received a prescription for a systemic antimicrobial.³⁷ This difference is partly because

PBS/RPBS data also include prescriptions generated by specialist doctors, non-medical prescribers and hospitals. The voluntary nature of the MedicineInsight program may also select for prescribers who are more likely to follow national guidelines.

Antimicrobial use in the community setting in Australia is very high compared with OECD member countries. In 2015, 45% of the population was dispensed at least one systemic antimicrobial, with an overall rate of 25.4 defined daily doses per 1,000 inhabitants per day.

The number of antimicrobial prescriptions dispensed peaked in 2008 at 25.5 DDDs per 1,000 inhabitants per day, which is similar to the rate reported in 2015. Since 2008, there has been no change in overall rates of prescriptions dispensed from year to year.

Penicillins are the most commonly prescribed antimicrobial group, and amoxicillin and amoxicillin-clavulanate are the most commonly prescribed agents in this group. There is minimal prescribing of narrow-spectrum penicillins; flucloxacillin is the most commonly prescribed agent in this class. The number of amoxicillin prescriptions dispensed has decreased slightly since 2008, and prescriptions dispensed for cefalexin and amoxicillin-clavulanate have continued to increase.

Australia relies heavily on β -lactams for treating infections in the community. During 2015, 69% of all prescriptions dispensed on the PBS/RPBS in Australia were for β -lactams. Only 8.3% of those β -lactams were for narrow-spectrum penicillins, meaning that 82% of β -lactams or 57% of all antimicrobials dispensed were moderate- and broad-spectrum β -lactams, which are likely to generate greater selective pressure for resistance.

Variations in prescribing

Data from both MedicineInsight and ROGS indicate variations in prescribing across states and territories, between major cities and other regions, and across socioeconomic status groups. Greater use of antimicrobials in areas of lower socioeconomic status is consistent with the poorer health and higher infection rates associated with lower socioeconomic status. However, there is insufficient evidence to identify the factors that are driving geographic patterns of antimicrobial prescribing in Australia. For many of the common bacteria involved in community-acquired infections, rates of resistance do not vary across the country.

Prescribing for upper respiratory tract infections

The proportion of acute upper respiratory tract infection presentations for which systemic antimicrobials were prescribed by general practitioners decreased from 32.4% over the five-year period April 2006 to March 2011 to 30.2% over the five-year period April 2010 to March 2015. Results varied across states and territories.⁹ This may be in response to the NPS MedicineWise antibiotic campaign that started in 2012, targeting clinicians and consumers.³⁹ However, high volumes of antimicrobials continue to be prescribed unnecessarily for respiratory tract infections. MedicineInsight data show that 60% of patients who presented to a general practitioner who contributed to MedicineInsight, where the reason for the visit was documented as colds and other upper respiratory tract infections, had an antimicrobial prescribed where no indication was recorded in the fields examined. A large proportion of patients with acute tonsillitis, acute or chronic sinusitis, acute otitis media or acute bronchitis appear to be prescribed an antimicrobial, when antimicrobial treatment should be the exception, not routine therapy.³⁷ The data further suggest that a proportion of antimicrobials prescribed were not those recommended by *Therapeutic Guidelines: Antibiotic*.

High volumes of antimicrobials continue to be prescribed unnecessarily for respiratory infections.

Amoxicillin-clavulanate, the third most commonly dispensed antimicrobial in the community, is restricted on the PBS to infections where resistance to amoxicillin is suspected or proven. MedicineInsight data showed that around 14% of amoxicillin-clavulanate prescribing was for upper respiratory tract infections, where antimicrobials were not indicated, and 15%

was for sinusitis, where antimicrobials are only indicated in specific circumstances³⁷ (with amoxicillin the recommended antimicrobial in *Therapeutic Guidelines: Antibiotic*).²³

The number of prescriptions dispensed for agents used to treat upper respiratory tract infections fluctuates significantly between winter and summer. This variation is highest for amoxicillin, amoxicillin-clavulanate, macrolides and doxycycline, indicating potential misuse of these antimicrobials for the treatment of colds and influenza. This was most apparent in children in the 0–9-year cohort, where the rate of amoxicillin prescriptions dispensed was twice that of other age groups, and the seasonal variation was greater.

There is low use of narrow-spectrum antimicrobials in Australia. For example, only 8% of β -lactam prescriptions dispensed were narrow-spectrum agents – namely, β -lactamase-sensitive penicillins. This contrasts with Scandinavian countries, where β -lactamase-sensitive penicillins were the most commonly prescribed antimicrobial class.^{40–42}

Repeat prescriptions

Repeat prescriptions are frequently ordered for commonly prescribed antimicrobials, such as amoxicillin and cefalexin, where a repeat prescription is not needed to complete a treatment course.³² In addition, previous PBS reports have noted that 10–20% of repeat prescriptions are dispensed many months after the date of prescribing, which is unlikely to be for the same course of treatment. Reducing unnecessary repeat prescriptions could be a target for community-based AMS.

Gaps and improvements

Improving antimicrobial usage data

Since April 2012, the PBS/RPBS data on volume of antimicrobial prescriptions dispensed through the PBS/RPBS have not included antimicrobials dispensed as private prescriptions. Future

reports would be improved if this information could be included, in addition to selected information from practice notes.

Presenting data on individual antimicrobials using measures such as DDDs per 1,000 inhabitants per day and prescriptions per 1,000 inhabitants would facilitate comparisons of AU in Australia with that in other countries.

In future AURA reports, analysis of public hospital PBS/RPBS data would provide useful information on antimicrobials dispensed to outpatients and discharged patients. It may also be useful to superimpose peak influenza years, national education programs and other national AMS interventions onto a graph of AU. This would help identify trends and points of impact that affect AU over time.

Strengthening antimicrobial stewardship

The Antimicrobial Stewardship Clinical Care Standard contains a quality statement on documenting the indication for prescribing antimicrobials.⁴³ In addition, the clinical care standard includes quality statements on the importance of microbiological testing to guide choice of antimicrobials, prescribing in accordance with the current version of *Therapeutic Guidelines: Antibiotic*, and documentation of a review or stop date. The clinical care standard should be broadly promoted and adopted in community and primary care.

Setting targets for antimicrobial prescribing in the community setting has been shown to influence antimicrobial prescribing in other countries, and could be considered for Australia.

3.3 Developments and future plans

Aged care homes

Aged care homes are recognised nationally and internationally as an important community setting for monitoring AMR and AU, because of the significant burden of infection and colonisation with resistant organisms. International and Australian data have demonstrated high levels of unnecessary antimicrobial prescribing and inappropriate antimicrobial use in this setting.⁴⁴

Establishment of approaches to AMS that are evidence based, best practice and nationally consistent across settings, including aged care homes, is a priority area for national action in Australia.¹

The Australian Government requires aged care homes that receive government subsidies to meet accreditation quality standards to ensure that the best care possible is provided to aged care residents.⁴⁵ Within the Aged Care Accreditation Standards, Standard 2 (Health and personal care) requires that medication management is safe and accurate. This requirement means that aged care homes should have effective AMS programs (or similar) in place. In the United States, it has been mandatory since September 2016 for long-term residential aged care homes that receive Medicare and Medicaid funding for aged care to establish an AMS program that includes AU protocols and a system to monitor AU.⁴⁶

To support development of sustainable and standardised survey instruments to monitor the prevalence of infections and AU in Australian aged care homes, the Commission funded the National Centre for Antimicrobial Stewardship to develop and pilot the Aged Care National Antimicrobial Prescribing Survey (acNAPS) in 2015.

The long-term objective of acNAPS is to support the implementation of AMS programs in aged care homes to monitor the prevalence of infections and the appropriateness of antimicrobial prescribing. After a successful pilot in 2015, acNAPS was launched in 2016 as an annual survey. Over time, it is anticipated that acNAPS data will help to identify priority areas for local, state and territory, and national quality improvement interventions to increase appropriate AU in Australian aged care homes.

As reported in AURA 2016 and in the acNAPS pilot report, 186 aged care homes and multi-purpose services participated in the acNAPS pilot between 22 June and 31 August 2015.⁴⁷ Almost 70% of participating sites were in Victoria, possibly because Victorian aged care homes had previously participated in similar state-based point prevalence surveys and were familiar with the data collection requirements.

Summary findings from the 2015 acNAPS pilot showed that the prevalence of residents with signs and symptoms of infection was 4.5%. The prevalence of residents prescribed one or more antimicrobials was 11.3%. In total, 975 antimicrobials were prescribed for 824 residents.

The five most commonly prescribed antimicrobials were cefalexin (16.7%), clotrimazole (16.5%), amoxicillin-clavulanate (6.5%), trimethoprim (6.5%) and chloramphenicol (6.4%).

Topical antimicrobials were frequently prescribed (37.1% of all antimicrobials). The five most common indications for antimicrobial prescribing were 'unspecified' skin, soft tissue or mucosal infections (17.5%); urinary tract infections (16.7%); lower respiratory tract infections (11.8%); tinea (8.4%); and conjunctivitis (5.2%).

Three key areas for targeted quality improvement interventions identified from the 2015 acNAPS pilot were:

- Inadequate documentation – 31.6% of prescriptions did not have an indication documented to justify their use, and 65.0% of prescriptions did not have a review or stop date documented
- Use of antimicrobials for unspecified infections – 17.5% of antimicrobials were being used for unspecified skin infections
- Prolonged duration of prescriptions – 31.4% of prescriptions had been prescribed for longer

than six months; of these, only 51.0% had an indication documented and only 2.0% had a review or stop date recorded.

The results of the 2015 acNAPS were widely communicated to the aged care sector by the National Centre for Antimicrobial Stewardship and the Commission.

The 2016 acNAPS was conducted between 27 June and 9 September 2016. The analysis of the 2016 acNAPS will be published by the Commission in collaboration with the National Centre for Antimicrobial Stewardship in 2017.

● From information to action

Expanding antimicrobial stewardship in aged care homes

The Grampians Region Infection Control Group (GRICG) is committed to delivering best-practice health care in its 34 aged care homes, and takes a proactive approach to quality improvement activities. The aim of its antimicrobial stewardship (AMS) program is to minimise infections and inappropriate antimicrobial use (AU), and thereby reduce the risk of antimicrobial resistance.

In 2015, the GRICG expanded its AMS program by participating in the pilot of the Aged Care National Antimicrobial Prescribing Survey (acNAPS) with the intention of monitoring the prevalence of infections and identifying inappropriate AU. The results of the 2015 pilot acNAPS were reported to clinical and administrative staff, off-site general practitioners, and pharmacists to educate residents and staff of aged care homes about infections and appropriate AU. The results also provided an evidence base to make necessary changes in clinical policy and practice.

The data from the acNAPS pilot also enabled each aged care home in the Grampians region to assess its appropriateness of antimicrobial prescribing against regional and national aggregates.

The GRICG intends to participate in acNAPS every year to monitor and evaluate the effectiveness of its AMS program. Data from acNAPS will also be used to assess the effectiveness of other AMS strategies, such as:

- A urinary tract infection (UTI) clinical pathway that was developed to increase the accuracy of clinical diagnosis of UTIs, optimise the use of microbiological services, and reduce inappropriate prescribing of antimicrobials for residents with asymptomatic bacteriuria
- Education sessions and study days aimed at educating the region's infection control liaison nurses about core infection control topics, including standard and transmission-based precautions in practice, outbreak management, and AMS more broadly.

Surgical antimicrobial prophylaxis

A large body of evidence supports appropriate AU for surgical prophylaxis to reduce surgical site and other postoperative infections. Guidance for surgical antimicrobial prophylaxis in Australia is available in *Therapeutic Guidelines: Antibiotic*.²³

Successive Hospital NAPS reports from 2013 to 2015 have shown that surgical prophylaxis is the most common indication for prescribing antimicrobials in public and private hospitals (11.5% in 2013, 13.1% in 2014 and 15.5% in 2015).^{22,48,49} During that time, the Hospital NAPS has also shown sustained levels of inappropriate prescribing of antimicrobials for surgical prophylaxis. In 2015, the most commonly identified reasons for inappropriateness were incorrect duration (29.9%), incorrect dose (27.6%) and the procedure not requiring antimicrobials (22.0%).

The results of the 2015 Hospital NAPS showed a reduction over the three years in the proportion of surgical prophylaxis prescriptions prescribed for longer than 24 hours – 27.4% in 2015, 35.9% in 2014 and 41.8% in 2013 (Figure 3.25). It is unclear whether this improvement is because of the increased number of participating hospitals, variations in casemix between public and private hospitals, or a real decrease in inappropriate prescribing. Although this decrease is encouraging, 27.4% remains significantly higher than the best-practice target of 5% or less.

Despite the reduction in the proportion of surgical prophylaxis prescriptions prescribed for longer than 24 hours, the rate of inappropriateness for surgical prophylaxis prescriptions remained fairly steady from 2013 to 2015 (41.6% in 2013, 40.0% in 2014 and 40.5% in 2015). This indicates that there may be other

Area for action

Intensify efforts to reduce unnecessary prescribing in the community

Australia continues to have very high overall rates of community antimicrobial use compared with a number of comparable countries. In 2015, around half of the Australian population (44.7%, about 10.7 million people) had at least one antimicrobial dispensed under the Pharmaceutical Benefits Scheme (PBS) or the Repatriation Pharmaceutical Benefits Scheme (RPBS). Many antimicrobial prescriptions in the community are unnecessary because antimicrobials are frequently used to treat infections for which they provide little or no benefit.

AURA 2017 supports the recommendations of the *Australian Atlas of Healthcare Variation* with regard to antimicrobial dispensing, and the Antimicrobial Stewardship Clinical Care

Standard. These include national benchmarks for prescribing antimicrobials, examination by the Pharmaceutical Benefits Advisory Committee (PBAC) of use of amoxicillin-clavulanate, and implementation of antimicrobial stewardship programs in general practice to reduce the use of amoxicillin, amoxicillin-clavulanate and cefalexin.

The AURA National Coordination Unit will work with the Australian Government Department of Health to develop national benchmarks for best-practice prescribing of antimicrobial agents. The Australian Commission on Safety and Quality in Health Care will also work with the PBAC to examine appropriate access to amoxicillin-clavulanate on the PBS/RPBS, given that the bulk of prescribing of this antimicrobial is for conditions that do not require an antimicrobial, or for which amoxicillin alone is recommended in national guidelines.

reasons, not yet identified, that contribute to this sustained level of inappropriateness.

In response to the high levels of inappropriate prescribing of antimicrobials for surgical prophylaxis, the Commission provided funding to the National Centre for Antimicrobial Stewardship to develop and pilot a dedicated Surgical NAPS (SNAPS) audit tool in 2015. As reported in AURA 2016, data from the 2015 SNAPS pilot confirmed findings of high rates of inappropriate prescribing that were previously identified by the Hospital NAPS (Figure 3.26).

The Commission subsequently supported the National Centre for Antimicrobial Stewardship to develop and pilot an online SNAPS module between April and October 2016. The results of the 2016 SNAPS will be published by the Commission in collaboration with the National Centre for Antimicrobial Stewardship in 2017.

Actions

The Commission continues to work in partnership with the National Centre for Antimicrobial Stewardship, the Royal Australasian College of Surgeons, and state and territory health authorities to investigate opportunities to improve prescribing and target education for surgical prophylaxis. Areas of focus are prolonged duration of therapy, incorrect dosing, and high rates of inappropriate prescribing of cefalexin.

In addition, the Commission is developing an accreditation advisory that will require inclusion of surgical prophylaxis as a component of AMS plans. The accreditation advisory is being developed in consultation with the Royal Australasian College of Surgeons, the Australian and New Zealand College of Anaesthetists, and state and territory health authorities.

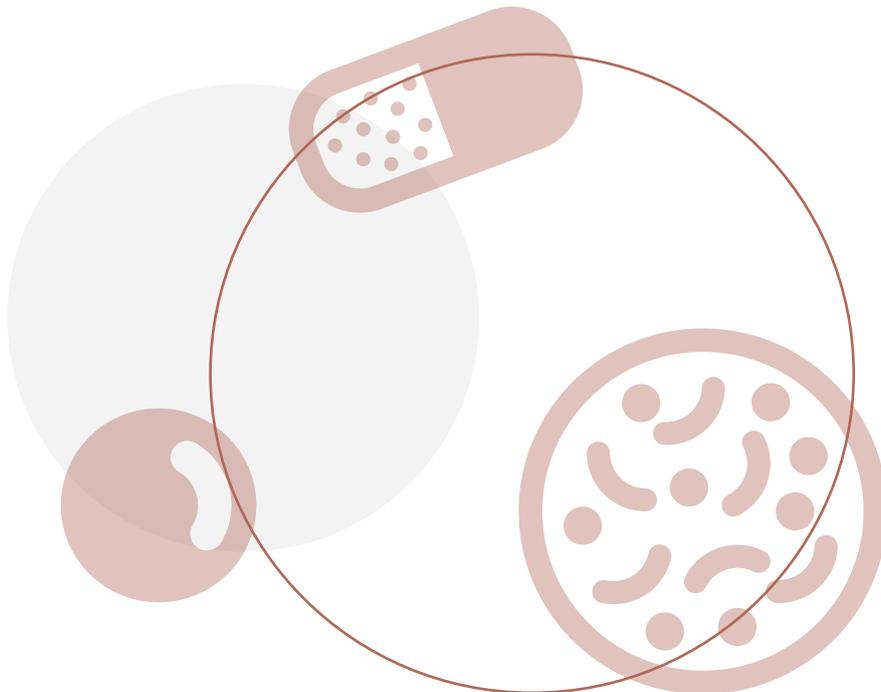
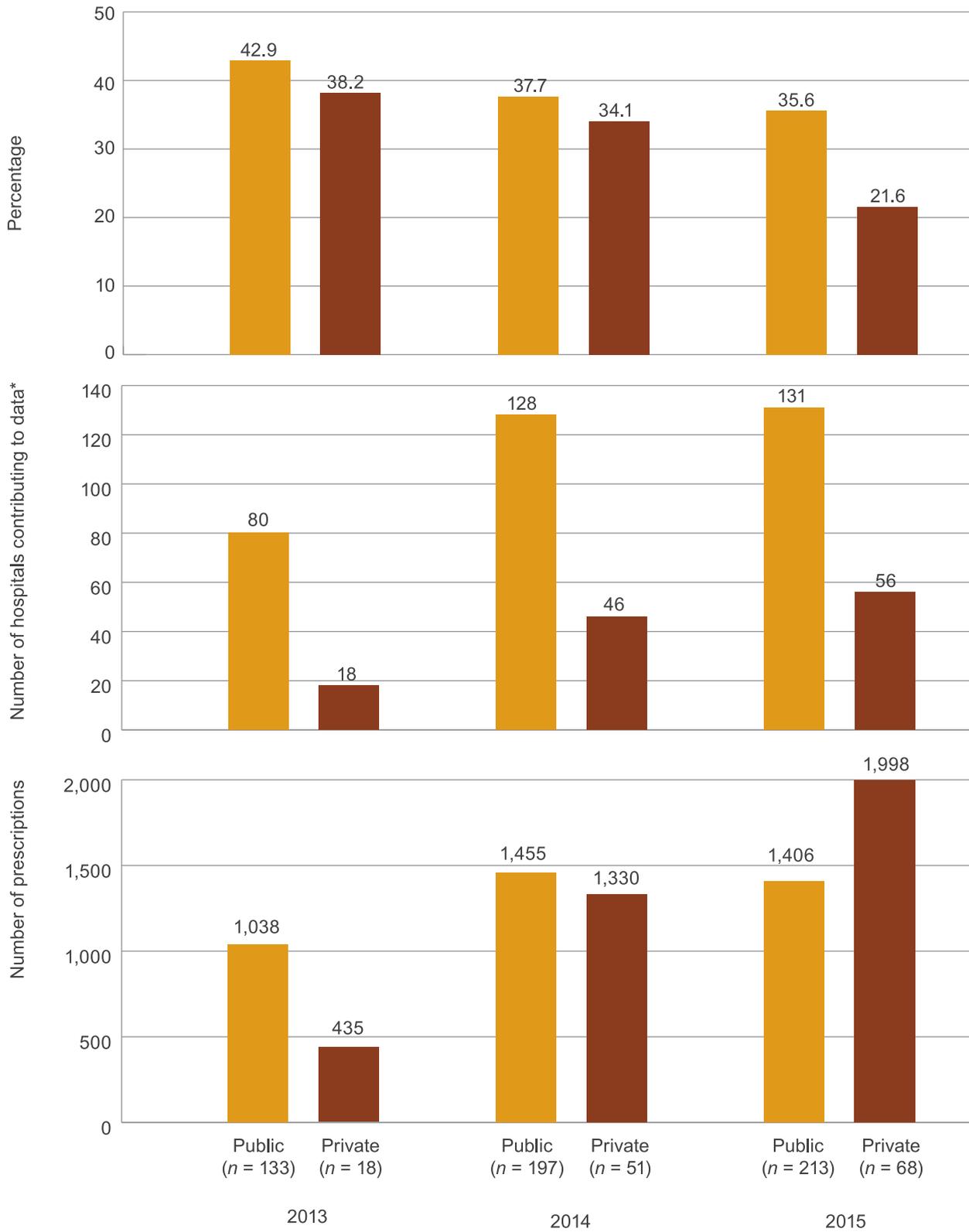


Figure 3.25: Surgical prophylaxis given for >24 hours, by hospital funding type, 2013–2015

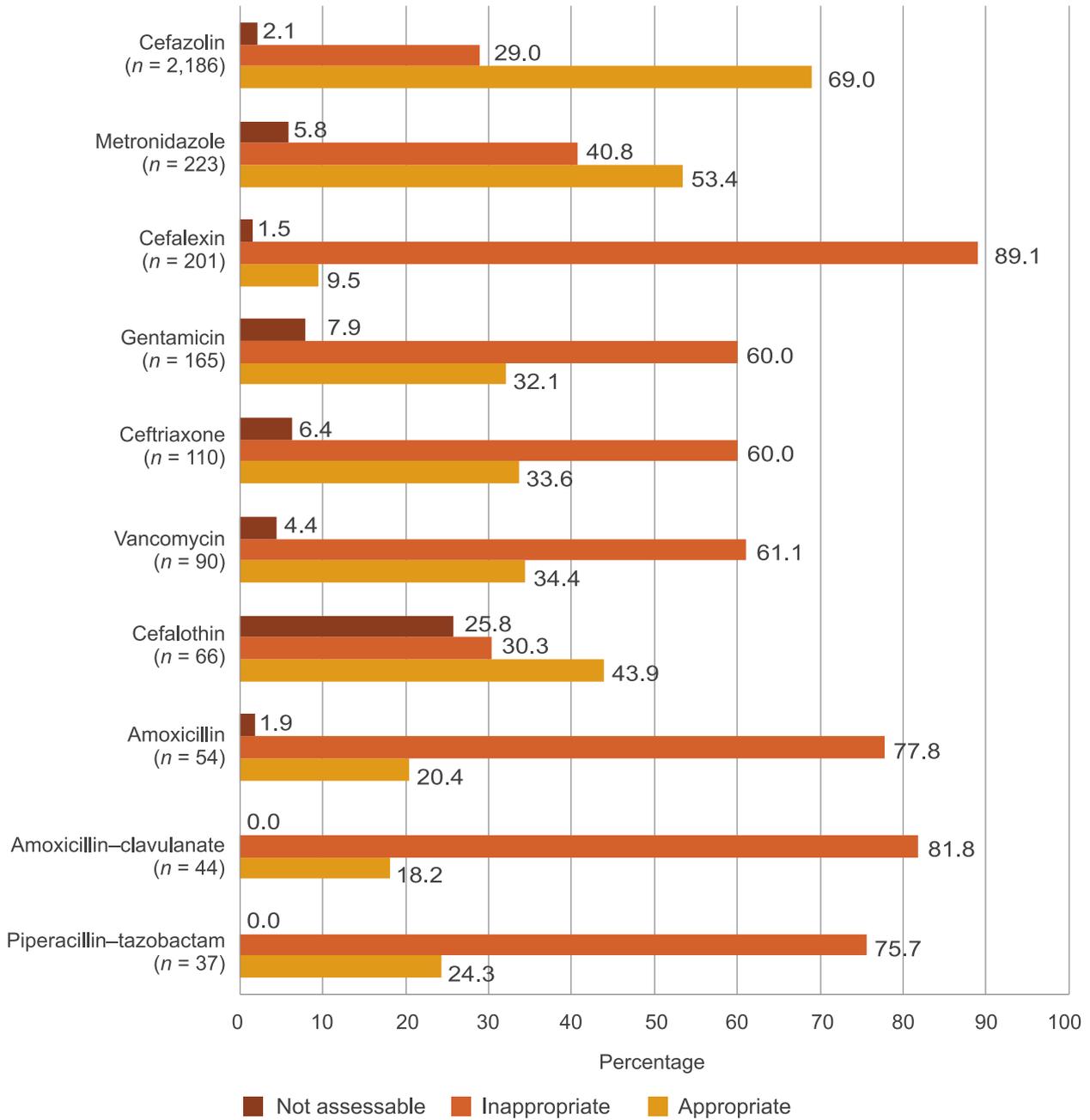


* Number of hospitals that had at least one antimicrobial prescribed for surgical prophylaxis

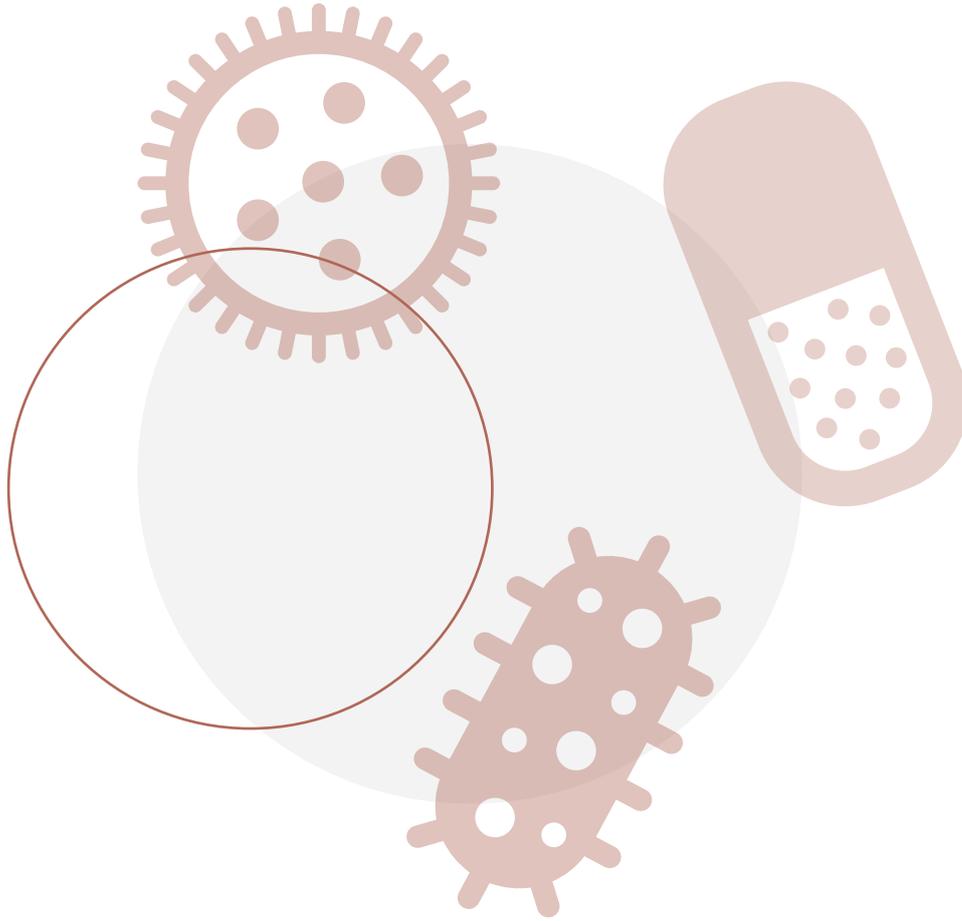
Note: Results are shown as a percentage of all surgical prophylaxis prescriptions. The number of contributing hospitals (n) is given in brackets.

Source: NAPS²²

Figure 3.26: The 10 most commonly prescribed antibacterials for surgical prophylaxis in NAPS contributor hospitals and appropriateness of prescribing, 2015



Source: NAPS²²





Chapter 4

Antimicrobial resistance

Key messages

- While there has been a major expansion in national data coverage, there have been few changes in resistance rates compared with 2014. Noticeable increases were seen in rates of fluoroquinolone resistance in *Escherichia coli* and *Shigella sonnei*, and reduced susceptibility and resistance to benzylpenicillin in *Neisseria meningitidis*.
- *Acinetobacter baumannii* – rates of resistance are low overall (<5%), and higher in public hospitals than in private hospitals or the community.
- Enterobacteriaceae – quinolone-resistant *E. coli* and extended-spectrum β -lactamase-producing *E. coli*, which are resistant to third-generation cephalosporins, are an increasing problem in community infections, as strains are often multidrug resistant.
- *Enterococcus* species – Australia has one of the highest rates of vancomycin resistance in *E. faecium* in the world. Rates of resistance to key antimicrobial agents are very low (<1%) in *E. faecalis*, but high (49–96%) in *E. faecium*.
- *Mycobacterium tuberculosis* – overall resistance rates have not changed significantly in the past decade. The rate of multi-drug resistance is low, but has been gradually increasing (1.9% in 2015); extremely drug-resistant strains are occasionally found but remain rare.
- *Neisseria gonorrhoeae* – rates of resistance to benzylpenicillin and ciprofloxacin remain steady at around 20–30%. Rates of resistance to azithromycin and decreased susceptibility to ceftriaxone are low but gradually increasing.
- *Neisseria meningitidis* – rates of resistance to the four key antimicrobials remain low (0–3%), although the rate of reduced susceptibility to benzylpenicillin is now 26%.

- *Pseudomonas aeruginosa* – overall rates of resistance to key antimicrobials are 10% or less; rates are higher in public hospitals than in other settings.
- *Salmonella* species – rates of resistance to fluoroquinolones are very low (1%) in non-typhoidal *Salmonella* species, but more than 50% in typhoidal *Salmonella* species.
- *Shigella* species – although data are limited, the presence of ciprofloxacin resistance in 20.3% of *S. sonnei* isolates is of concern.
- *Staphylococcus aureus* – between 10.7% and 30.8% of isolates are methicillin-resistant *S. aureus* (MRSA), depending on the setting. Community strains of MRSA now cause a significant proportion of infections in both the community and hospitals.
- *Streptococcus agalactiae* – no isolates were resistant to benzylpenicillin, but resistance to erythromycin and clindamycin exceeds 20%. Protocols for prophylaxis may need to be reconsidered.
- *Streptococcus pneumoniae* – resistance (as defined for strains causing infections other than meningitis) to benzylpenicillin is low (2.8–4.6%), but resistance to other key antimicrobials is 16–26%.
- *Streptococcus pyogenes* – resistance to key antimicrobials used for treatment is absent or very low (4%).

This chapter provides the results of the analyses of data collected from the passive and targeted components of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System from hospitals, aged care homes and the general community. The results have been compiled for each of the 13 priority organisms in AURA.

4.1 Introduction

Antimicrobial-resistant bacteria and their resistance genes can spread readily between people in the community, primary care services, hospitals and aged care homes. This can happen rapidly, and often go unnoticed. The spread of these bacteria can significantly affect the community, patients, health services and the health system. Therefore, it is critical that resistant bacteria with the highest risk of causing harm to humans are identified and monitored through enhanced surveillance, and managed appropriately.

Priority organisms for surveillance

To focus Australia’s antimicrobial resistance (AMR) surveillance efforts, the Australian Commission on Safety and Quality in Health Care (the Commission) developed a list of organisms and key antimicrobials that are high priorities for AMR strategies in Australia. Key experts involved in the AURA project advised on the development of this list.

Priority organisms are those of high public health importance and/or common pathogens where the impact of resistance is substantial in both the hospital and community settings.

The surveillance of these organisms is coordinated by the Commission across several programs that are now part of AURA. AURA 2016 provided data on these organisms for the first time at a national level. AURA 2017 provides additional data to strengthen the picture of

rates of resistance, commentary on some related outcome measures and an assessment of trends over time, where sufficient data are available. The Commission continues to direct, coordinate and report on this enhanced surveillance to support improvements in Australia's capacity to prevent and contain AMR.

The priority organism list (Appendix 2) comprises four sets of organisms. AURA reports on organisms in sets 1 and 2, and set 4, where sufficient data are available:

- *Acinetobacter baumannii*
- Enterobacteriaceae
- *Enterococcus* species
- *Mycobacterium tuberculosis*
- *Neisseria gonorrhoeae*
- *Neisseria meningitidis*
- *Pseudomonas aeruginosa*
- *Salmonella* species
- *Shigella* species
- *Staphylococcus aureus*
- *Streptococcus agalactiae*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*.

Sets 3 and 4 include organisms that require further development of surveillance capacity, or that have been identified as organisms to monitor for potential inclusion in future surveillance activity.

The priority list will continue to be reviewed and updated by the Commission as new data become available.

Data on priority organisms

This report includes data from:

- The National Passive AMR Surveillance System (using the infrastructure of the Queensland Health OrgTRx system), which collects data from public hospitals and health services across Queensland, New South Wales, the Australian Capital Territory, Victoria, Tasmania,

Western Australia and South Australia, as well as one private hospital in Queensland and some private hospitals in South Australia

- The Sullivan Nicolaides Pathology information system, which collects data from its own laboratories in Queensland and northern New South Wales; these laboratories service private hospitals, community-based services and aged care homes
- The Australian Group on Antimicrobial Resistance (AGAR), which collects data on minimum inhibitory concentrations (MICs) of antimicrobials from laboratories across Australia for selected organism groups, as well as some demographic and outcome data, and undertakes additional characterisation of strains
- The National Neisseria Network (NNN), which collects data and undertakes confirmatory susceptibility testing for all *N. gonorrhoeae* and *N. meningitidis* cases across Australia
- The National Notifiable Diseases Surveillance System (NNDSS), which collects susceptibility testing data for all confirmed *M. tuberculosis* cases across Australia.

Additional tables with more detailed information are provided in *AURA 2017: Supplementary data*. Also see Appendix 1 for an overview of each data source program and a link to its website for further information.

The coordinating role of the Commission will ensure that the AURA Surveillance System monitors changes in the nature of AMR for each organism. The Commission will include this information in regular reporting.

Table 4.1 provides a summary of the data sources for each organism, and Table 4.2 summarises the priority organisms and their AMR prevalence. Table 4.2 shows some changes in the prevalence of resistance in some organisms from 2014 to 2015. Increases were noted in ciprofloxacin-resistant and multidrug-resistant *E. coli*, vancomycin-resistant *Enterococcus*

Table 4.1: Data sources for priority organisms included in this report

Section of report	Organism	Data source
4.2	<i>Acinetobacter baumannii</i>	<ul style="list-style-type: none"> National Passive AMR Surveillance System (OrgTRx)* - public hospitals and health services nationally (except NT and WA), one private hospital in Qld and several private hospitals in SA SNP⁺ - Qld and northern NSW communities, private hospitals and aged care homes AGAR[§] - national public and private hospitals
4.3	Enterobacteriaceae	<ul style="list-style-type: none"> National Passive AMR Surveillance System (OrgTRx)* - public hospitals and health services nationally (except NT and WA), one private hospital in Qld and several private hospitals in SA SNP⁺ - Qld and northern NSW communities, private hospitals and aged care homes AGAR[§] - national public and private hospitals
4.4	<i>Enterococcus faecalis</i> and <i>E. faecium</i>	<ul style="list-style-type: none"> National Passive AMR Surveillance System (OrgTRx)* - public hospitals and health services nationally (except NT and WA), one private hospital in Qld and several private hospitals in SA SNP⁺ - Qld and northern NSW communities, private hospitals and aged care homes AGAR[§] - national public and private hospitals
4.5	<i>Mycobacterium tuberculosis</i>	<ul style="list-style-type: none"> NNDSS^{#,**} - national hospitals and community health services
4.6	<i>Neisseria gonorrhoeae</i>	<ul style="list-style-type: none"> NNN[‡] - national hospitals and community health services
4.7	<i>Neisseria meningitidis</i>	<ul style="list-style-type: none"> NNN - national hospitals and community health services
4.8	<i>Pseudomonas aeruginosa</i>	<ul style="list-style-type: none"> National Passive AMR Surveillance System (OrgTRx)* - public hospitals and health services nationally (except NT and WA), one private hospital in Qld and several private hospitals in SA SNP⁺ - Qld and northern NSW communities, private hospitals and aged care homes AGAR[§] - national public and private hospitals
4.9	<i>Salmonella</i> species	<ul style="list-style-type: none"> National Passive AMR Surveillance System (OrgTRx)* - public hospitals and health services nationally (except NT and WA), one private hospital in Qld and several private hospitals in SA SNP⁺ - Qld and northern NSW communities, private hospitals and aged care homes AGAR[§] - national public and private hospitals
4.10	<i>Shigella</i> species	<ul style="list-style-type: none"> National Passive AMR Surveillance System (OrgTRx)* - public hospitals and health services nationally (except NT and WA), one private hospital in Qld and several private hospitals in SA SNP⁺ - Qld and northern NSW communities, private hospitals and aged care homes
4.11	<i>Staphylococcus aureus</i>	<ul style="list-style-type: none"> National Passive AMR Surveillance System (OrgTRx)* - public hospitals and health services nationally (except NT and WA), one private hospital in Qld and several private hospitals in SA SNP⁺ - Qld and northern NSW communities, private hospitals and aged care homes AGAR[§] - national public and private hospitals

continued

Table 4.1: continued

Section of report	Organism	Data source
4.12	<i>Streptococcus agalactiae</i>	<ul style="list-style-type: none"> National Passive AMR Surveillance System (OrgTRx)* - public hospitals and health services nationally (except NT and WA), one private hospital in Qld and several private hospitals in SA SNP[†] - Qld and northern NSW communities, private hospitals and aged care homes
4.13	<i>Streptococcus pneumoniae</i>	<ul style="list-style-type: none"> National Passive AMR Surveillance System (OrgTRx)* - public hospitals and health services nationally (except NT and WA), one private hospital in Qld and several private hospitals in SA SNP^{†,§§} - Qld and northern NSW communities, private hospitals and aged care homes
4.14	<i>Streptococcus pyogenes</i>	<ul style="list-style-type: none"> National Passive AMR Surveillance System (OrgTRx)* - public hospitals and health services nationally (except NT and WA), one private hospital in Qld and several private hospitals in SA SNP[†] - Queensland and northern NSW communities, private hospitals and aged care homes

AGAR = Australian Group on Antimicrobial Resistance; AMR = antimicrobial resistance; NNDSS = National Notifiable Diseases Surveillance System; NNN = National Neisseria Network; SNP = Sullivan Nicolaides Pathology

* For antimicrobials where ≥75% of isolates were tested using either the European Committee on Antimicrobial Susceptibility Testing (EUCAST) or Clinical and Laboratory Standards Institute (CLSI) interpretive criteria, and at least 30 strains were tested. In 2015, ACT and Vic used CLSI, NSW and SA changed from CLSI to EUCAST, and Qld and Tas used EUCAST.

† For antimicrobials where ≥75% of isolates were tested using the EUCAST interpretive criteria, and at least 30 strains were tested.

§ National data from AGAR using EUCAST interpretive criteria (except for cefazolin, where CLSI interpretive criteria were used).

All Australian Mycobacterium Reference Laboratory Network laboratories that provide data to the NNDSS now use the same commercial broth system for susceptibility testing for *M. tuberculosis*, but different susceptibility testing methods have been used in the past in some laboratories. For the purposes of reporting historical trend data, the results of other methods have been assumed to be equivalent.

** All laboratories in the network test every isolate against the four first-line agents. Tests against additional antimycobacterial agents are conducted when (1) resistance to isoniazid and rifampicin is detected, (2) resistance to two or more first-line agents is detected, and (3) patients experience severe adverse reactions to first-line agents. Interpretive criteria for resistance are currently those of the CLSI.

‡ Most cases of gonococcal infection are now diagnosed using nucleic acid techniques, and specimens for culture are not collected. Because current susceptibility testing methods depend on obtaining a culture of the organism, only a minority of cases undergo susceptibility testing.

§§ There were insufficient data to report the prevalence of resistance for strains causing meningitis.

Table 4.2: Summary of antimicrobial resistance for high-priority organisms

Organism	Main types of infection	Where seen	Important antimicrobials for treatment	% resistant, 2014	% resistant, 2015
<i>Acinetobacter baumannii</i>	Ventilator-associated pneumonia, severe burn infections	Intensive care units, burn units	Ciprofloxacin	4.1	3.1
			Gentamicin	2.4	1.6
			Meropenem	3.6	2.6
<i>Escherichia coli</i>	Urinary tract infections, biliary tract infections, other intra-abdominal infections, septicaemia	Community, hospitals	Amoxicillin-clavulanate	18.2-21.1	9.4-20.1
			Ampicillin/amoxicillin	42.3-51.3	42.9-53.2
			Cefazolin	15.2-25.0	15.8-24.8
			Ceftriaxone	5.1-12.4	6.4-10.8
			Ciprofloxacin	6.2-8.7	7.3-11.2
			Gentamicin	4.5-7.0	4.9-7.5
			Piperacillin-tazobactam	5.3-9.4	4.6-7.3
			Trimethoprim	21.0-29.4	21.8-31.3
			Multidrug resistant	13.1	23.7
<i>Enterobacter cloacae</i>	Urinary tract infections, other intra-abdominal infections, septicaemia	Hospitals	Ceftriaxone	23.8-28.5	22.8-36.2
			Piperacillin-tazobactam	24.3-32.2	19.5-26.6
			Trimethoprim	18.3-21.3	10.9-20.4
			Gentamicin	7.2-7.8	5.4-9.2
			Ciprofloxacin	3.7-5.2	3.1-6.2
			Meropenem	1.1-2.6	1.4-2.2
<i>Enterococcus faecalis</i>	Urinary tract infections, biliary tract infections, other intra-abdominal infections, septicaemia, endocarditis (heart valve infections)	Community, hospitals	Ampicillin	0.3-0.6	0.1-0.5
			Vancomycin	0.3-0.4	0.1-0.3
<i>Enterococcus faecium</i>	Urinary tract infections, biliary tract infections, other intra-abdominal infections, septicaemia	Hospitals	Ampicillin	83.3-94.5	86.3-95.9
			Linezolid	0.2-1.1	0.0-0.4
			Vancomycin	45.7-49.9	48.7-56.8

continued

Table 4.2: continued

Organism	Main types of infection	Where seen	Important antimicrobials for treatment	% resistant, 2014	% resistant, 2015
<i>Klebsiella pneumoniae</i>	Urinary tract infections, other intra-abdominal infections, septicaemia	Community	Amoxicillin-clavulanate	6.2-9.4	4.4-7.3
			Cefazolin	6.6-10.6	6.8-10.8
			Ceftriaxone	4.3-6.6	5.0-7.0
			Ciprofloxacin	4.5-6.2	3.7-4.8
			Gentamicin	3.1-4.9	3.2-4.2
			Piperacillin-tazobactam	7.6-8.9	6.0-7.7
			Trimethoprim	12.3-16.6	10.1-14.1
			Multidrug resistant	9.0	10.2
<i>Mycobacterium tuberculosis</i>	Pulmonary tuberculosis, extrapulmonary tuberculosis	Community	Ethambutol	1.2	0.9
			Isoniazid	8.5	10.7
			Pyrazinamide	2.1	2.7
			Rifampicin	2.4	3.8
			Multidrug resistant	1.7	1.9
<i>Neisseria gonorrhoeae</i>	Gonorrhoea	Community	Azithromycin	2.5	2.6
			Benzylpenicillin	28.5	22.5
			Ceftriaxone (decreased susceptibility)	5.4	1.8
			Ciprofloxacin	36.4	27.2
<i>Neisseria meningitidis</i>	Septicaemia	Community	Benzylpenicillin (decreased susceptibility)	15.8	25.6
			Ceftriaxone	0.0	0.0
			Ciprofloxacin	0.0	0.0
			Rifampicin	2.1	0.9
<i>Pseudomonas aeruginosa</i>	Urinary tract infections, burn infections, cystic fibrosis exacerbations	Community, hospitals	Ceftazidime	4.5	4.5
			Ciprofloxacin	6.7	6.2
			Gentamicin	5.3	5.2
			Meropenem	4.0	3.5
			Piperacillin-tazobactam	10.3	7.3
<i>Salmonella</i> species (non-typhoidal)	Gastroenteritis, septicaemia	Community	Ampicillin	6.7-7.7	1.6-7.1
			Ceftriaxone	0.6-1.9	0.0-1.5
			Ciprofloxacin	0.0-1.1	0.0-2.2
<i>Salmonella</i> Typhi/Paratyphi	Typhoid fever (septicaemia)	Community	Ampicillin	2.3	4.9
			Ceftriaxone	0.0	1.2
			Ciprofloxacin	12.2	51.4

continued

Table 4.2: continued

Organism	Main types of infection	Where seen	Important antimicrobials for treatment	% resistant, 2014	% resistant, 2015
<i>Shigella flexneri</i>	Bacillary dysentery	Community	Ampicillin	57.1	70.0
			Ceftriaxone	0.0	0.0
			Ciprofloxacin	0.0	0.0
<i>Shigella sonnei</i>	Bacillary dysentery	Community	Ampicillin	10.6	18.2
			Ceftriaxone	3.1	6.8
			Ciprofloxacin	9.4	20.3
<i>Staphylococcus aureus</i>	Skin, wound and soft tissue infections; bone and joint infections; device-related infections; septicaemia; endocarditis (heart valve infections)	Community, hospitals	Benzylpenicillin	83.1–88.7	83.2–87.7
			Clindamycin	7.1–10.0	8.1–14.6
			Erythromycin (and other macrolides)	16.5–17.0	14.4–17.0
			Oxacillin (methicillin)	15.8–17.4	11.8–15.0
<i>Staphylococcus aureus</i> (methicillin resistant)	Skin, wound and soft tissue infections; bone and joint infections; device-related infections; septicaemia; endocarditis (heart valve infections)	Community, hospitals	Clindamycin	14.2–19.6	22.9–23.7
			Fusidic acid	4.6–5.9	4.4–5.2
			Linezolid	0.1–0.3	0.0–0.1
			Rifampicin	0.8–0.9	0.8–1.9
			Trimethoprim-sulfamethoxazole	2.5–11.9	7.0–11.7
			Vancomycin	0.0	0.0
<i>Streptococcus agalactiae</i>	Skin and soft tissue infections, urinary tract infections, newborn septicaemia	Community	Benzylpenicillin	0.0	0.0
			Clindamycin	17.1	22.4
			Erythromycin (and other macrolides)	22.7	26.7
			Trimethoprim	17.2	13.9
<i>Streptococcus pneumoniae</i>	Otitis media (middle ear infections), sinusitis, acute exacerbation of chronic obstructive pulmonary disease, pneumonia, meningitis, septicaemia	Community	Benzylpenicillin (outside the central nervous system)	2.0–2.3	2.8–4.6
			Erythromycin (and other macrolides)	21.1–25.9	14.5–24.1
			Tetracycline (and doxycycline)	21.1–25.6	15.1–24.4
<i>Streptococcus pyogenes</i>	Skin, wound and soft tissue infections; septicaemia	Community	Benzylpenicillin	0.0	0.0
			Erythromycin (and other macrolides)	3.4	4.1
			Clindamycin	-	3.8

- = not reported (either not tested or tested against an inadequate number of isolates)

faecium, and benzylpenicillin-resistant *N. meningitidis*. Reports of ceftriaxone-resistant *N. gonorrhoeae* decreased.

4.2 *Acinetobacter baumannii* complex

This section describes the health impact, treatment, types and impact of resistance, and key findings for resistance rates in *A. baumannii*.

Health impact

The *A. baumannii* species complex is a group of environmental organisms that cause infections in patients with compromised physical barriers and immunity. The most common infections caused by this species complex are ventilator-associated pneumonia, and traumatic and burn wound infections. The species complex can cause sustained outbreaks in certain clinical settings, such as intensive care units and severe burn units.

Treatment

Because of its pattern of intrinsic resistances to many antimicrobial classes, the preferred agents to treat serious *A. baumannii* complex infections are carbapenems.

Types and impact of resistance

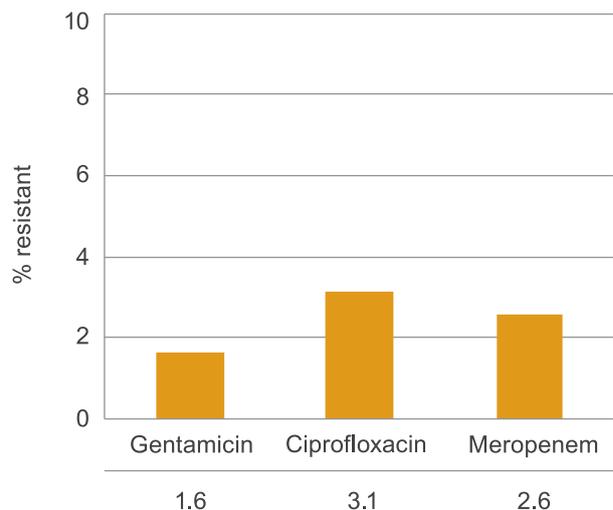
The members of *A. baumannii* complex have a high propensity for developing resistance to multiple antimicrobial agents, including broad-spectrum agents such as carbapenems. Sometimes, they are only susceptible to potentially toxic antimicrobials, such as colistin. Even this agent is a problem because of hetero-resistance (strains that naturally harbour resistant subpopulations), which requires combination treatment with other antimicrobials.

A. baumannii complex has a high propensity for developing resistance to multiple antimicrobial agents.

Key findings: national

Rates of resistance to key antimicrobial agents were low in 2015 (Figure 4.1) – almost always less than 5%. Resistance rates were higher in hospitals than in the community (Figure 4.2), which might be attributable to more resistant strains being established in some hospital units.

Figure 4.1: *Acinetobacter baumannii* complex resistance to individual agents, 2015



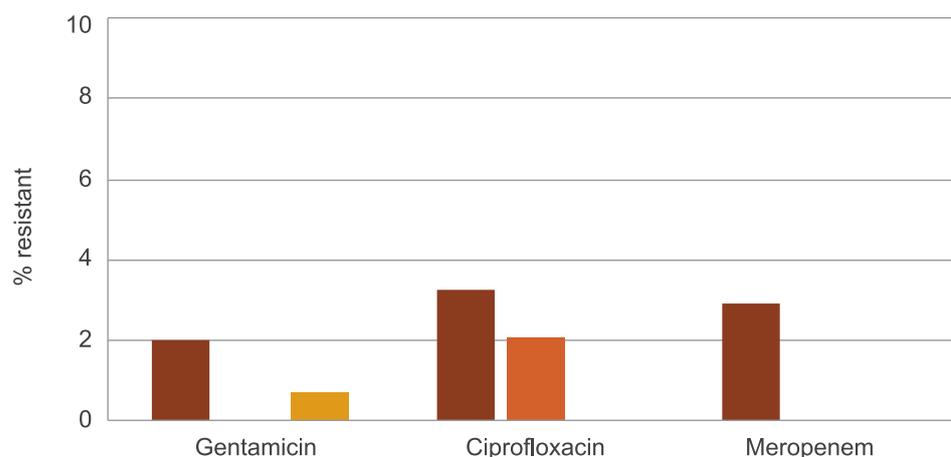
Note: $n = 1,121$

Sources: AGAR (national), National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

Key findings: states and territories

There was variation in rates of resistance to ciprofloxacin between states and territories (Figure 4.3).

Figure 4.2: *Acinetobacter baumannii* complex resistance, by clinical setting, 2015

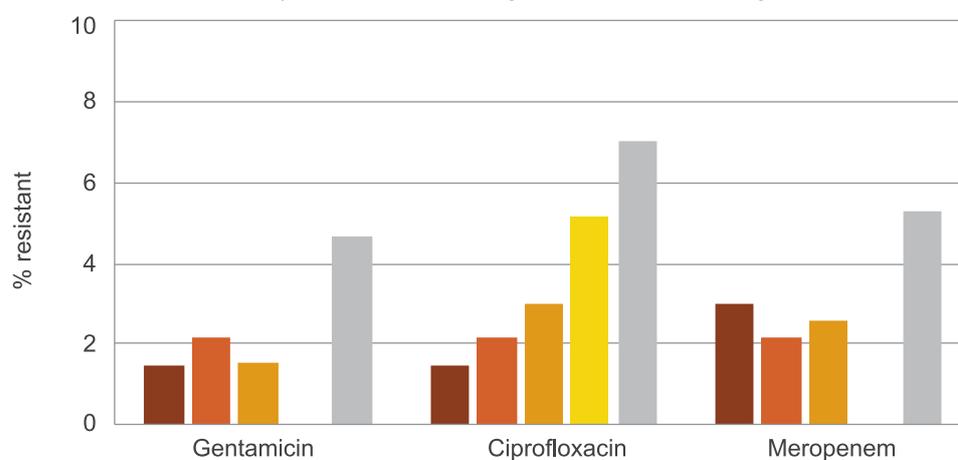


Public hospitals (n = 860)	2.0	3.2	2.9
Private hospitals (n = 113)	0.0	2.0	0.0
Community (n = 148)	0.7	-	-

- = not available (either not tested or tested against an inadequate number of isolates)

Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

Figure 4.3: *Acinetobacter baumannii* complex resistance, by state and territory, 2015



NSW (n = 68)	1.5	1.5	2.9
Vic (n = 47)	2.1	2.1	2.1
Qld (n = 924)	1.5	3.0	2.5
Tas (n = 39)	0.0	5.1	0.0
ACT (n = 43)	4.7	7.0	5.3

Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

4.3 Enterobacteriaceae

This section describes the health impact, treatment, types and impact of resistance, and key findings for resistance rates in Enterobacteriaceae.

Health impact

The Enterobacteriaceae family is a large group of related bacteria. Many of its members are associated with infections in humans. Of these, *E. coli* and *Klebsiella pneumoniae* are the most common and important species, and cause both community- and hospital-associated infections. *Enterobacter cloacae* complex is a common pathogen in hospital care. The Enterobacteriaceae family also includes *Salmonella* and *Shigella* species; these are reported on separately in Sections 4.9 and 4.10.

E. coli, *K. pneumoniae* and *E. cloacae* complex are associated with a range of infections, including

urinary tract infections, biliary infections, other intra-abdominal infections (including those following surgery, and often mixed with other pathogens) and septicaemia. In particular, *E. coli* is the most common cause of urinary tract infection and septicaemia in the community and in otherwise healthy people. Less frequently, the three species are a cause of bacteraemia from intravascular lines and meningitis.

Table 4.3 shows AGAR data for the most common clinical syndromes associated with Enterobacteriaceae. Urinary tract infections with these organisms are more common in females, whereas other clinical manifestations are more common in males.

Treatment

Beta-lactam agents, including those combined with β -lactamase inhibitors, are preferred for treatment of infections caused by these species. The aminoglycosides (especially gentamicin) are

Table 4.3: Principal clinical manifestations of infections with Enterobacteriaceae (all species, blood culture isolates), 2015

Principal clinical manifestation	Male	Female	Total
Urinary tract infection	895	1,192	2,087
Biliary tract infection (including cholangitis)	492	289	781
Intra-abdominal infection other than biliary tract	258	236	494
Other clinical syndrome	181	109	290
No focus (setting not known)*	150	135	285
Febrile neutropenia (when specified)*	153	109	262
No focus (setting known; e.g. in febrile neutropenia)*	45	28	73
Device-related infection without metastatic focus	88	48	136
Skin and skin structure infection	73	34	107
Osteomyelitis/septic arthritis	34	10	44
Device-related infection with metastatic focus	17	13	30
Total	2,386	2,203	4,589

* These principal clinical manifestations reflect the variation in reporting by contributors.

Source: AGAR (national)

also recommended, usually for empirical use, pending the results of culture and susceptibility testing. In Australia, fluoroquinolones are recommended only for strains that are resistant to other classes of antimicrobials. In addition to β -lactams, trimethoprim is recommended for treatment of lower urinary tract infection.

Types and impact of resistance

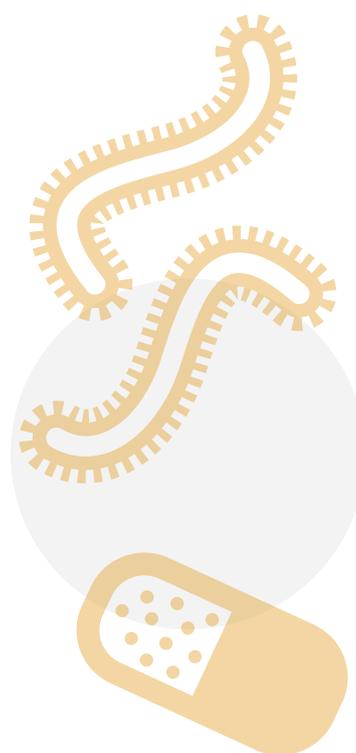
The most common resistance mechanisms in Enterobacteriaceae are β -lactamases. The acquired TEM1 β -lactamase has become so common worldwide that it is found in at least half of the strains isolated from humans in the community in Australia, making these strains resistant to ampicillin and amoxicillin. Both *K. pneumoniae* and *E. cloacae* complex contain intrinsic β -lactamases that make them naturally resistant to ampicillin/amoxicillin. In addition, the intrinsic β -lactamase of *E. cloacae* complex makes this species resistant to first-generation cephalosporins such as cefazolin and cefalexin, and the enzyme can be easily upregulated to make the species resistant to third-generation cephalosporins such as ceftriaxone, cefotaxime and ceftazidime. The β -lactam/ β -lactamase inhibitor combinations amoxicillin-clavulanate and piperacillin-tazobactam are the usual treatments for TEM1-producing *E. coli*, *K. pneumoniae* and *E. cloacae* complex, along with third-generation cephalosporins.

The acquired β -lactamases of greatest interest are the extended-spectrum β -lactamases (ESBLs), the plasmid-borne AmpC enzymes (pAmpCs) and the carbapenemases. ESBLs and pAmpCs render Enterobacteriaceae resistant to third-generation cephalosporins, and carbapenemases confer resistance to carbapenems and almost all other β -lactams. Carbapenemase-producing Enterobacteriaceae (CPE) are almost always highly multidrug resistant.

Other resistance mechanisms in Enterobacteriaceae that have clinical impact include the aminoglycoside-modifying enzymes,

which render strains resistant to gentamicin and tobramycin (but susceptible to amikacin), and the ribosomal methylases, which confer resistance to gentamicin, tobramycin and amikacin. Resistance to fluoroquinolones is usually through mutations at the target sites (the topoisomerases), but, recently, plasmid-borne resistance has emerged. Resistance to trimethoprim-sulfamethoxazole is common and occurs through a variety of mechanisms.

E. coli, *K. pneumoniae* and *E. cloacae* complex are noted for their capacity to acquire and transmit resistance genes among themselves and to some other genera through horizontal gene transfer. In addition, this family has specialised mechanisms (integrons) for capturing and accumulating resistance genes, giving them great capacity to become multidrug resistant. The number of agents available for treatment of highly multidrug-resistant strains is limited, and all these agents have greater toxicity than the β -lactams.



E. coli, *K. pneumoniae* and *E. cloacae* complex are noted for their capacity to acquire and transmit resistance genes among themselves and to some other genera through horizontal gene transfer.

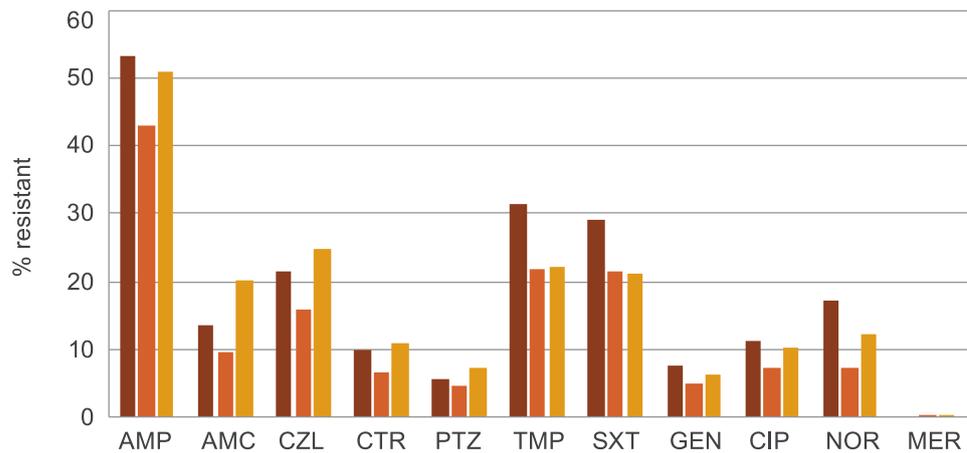
Key findings: national

In 2015, there continued to be no substantial differences in resistances between specimen sources for any of the three species that are reported on. Resistance to ampicillin (and amoxicillin) was the most common resistance in *E. coli*, and intrinsic in *K. pneumoniae* and *E. cloacae* complex. Resistance to amoxicillin-clavulanate occurred in 10–20% of *E. coli* and less than 10% of *K. pneumoniae* (Figures 4.4 and 4.6). Resistance to cefazolin and trimethoprim

(with or without sulfamethoxazole) was common in *E. coli*, but less so in *K. pneumoniae*. The ESBL phenotype was found in 6–12% of *E. coli* and 5–7% of *K. pneumoniae*. Resistance to third-generation cephalosporins (ceftriaxone) in *E. cloacae* complex was 24–36% (Figure 4.8), mostly due to stably derepressed mutants of its intrinsic cephalosporinase. The lower resistance rate to cefepime in this species (5.5%) is an indication of the proportion of this species that harbours ESBLs. Fluoroquinolone (ciprofloxacin, norfloxacin) resistance was detected in 7–17% of *E. coli*, 3–5% of *K. pneumoniae* and 3–7% of *E. cloacae* complex. Resistance to carbapenems (meropenem) was less than 0.5% in *E. coli* and *K. pneumoniae*, but 1–3% in *E. cloacae* complex (Figures 4.4, 4.6 and 4.8).

Rates of resistance were lower in the community for most agents, where data were available, than in hospitals. Rates in aged care homes were often as high as, or higher than, in hospitals (Figures 4.5, 4.7 and 4.9).

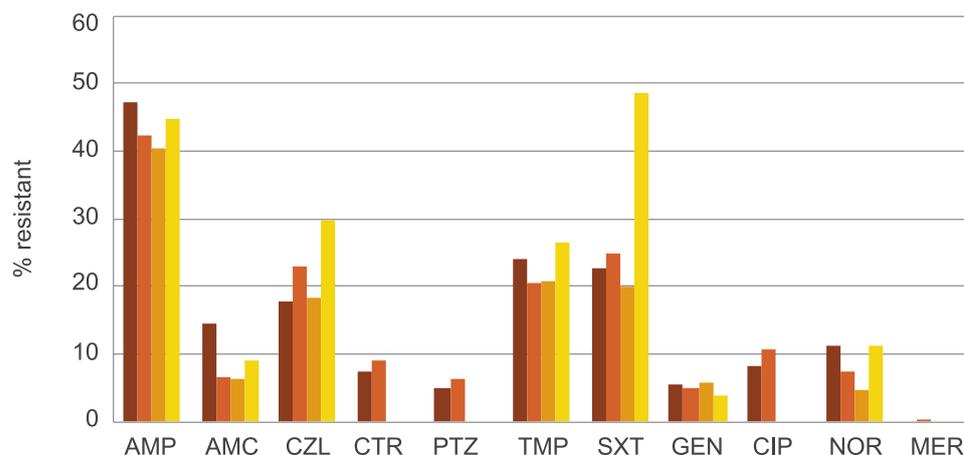
Figure 4.4: *Escherichia coli* resistance, by specimen source, 2015



■ Blood (n = 9,122)	53.2	13.5	21.5	9.8	5.6	31.3	29.1	7.5	11.2	17.0	0.0
■ Urine (n = 135,900)	42.9	9.4	15.8	6.4	4.6	21.8	21.3	4.9	7.3	7.1	0.0
■ Other (n = 5,973)	51.0	20.1	24.8	10.8	7.3	22.1	20.9	6.3	10.3	12.0	0.1

AMC = amoxicillin-clavulanate; AMP = ampicillin; CIP= ciprofloxacin; CTR = ceftriaxone; CZL = cefazolin; GEN = gentamicin; MER = meropenem; NOR = norfloxacin; PTZ = piperacillin-tazobactam; SXT = trimethoprim-sulfamethoxazole; TMP = trimethoprim
Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

Figure 4.5: *Escherichia coli* resistance, by clinical setting, 2015

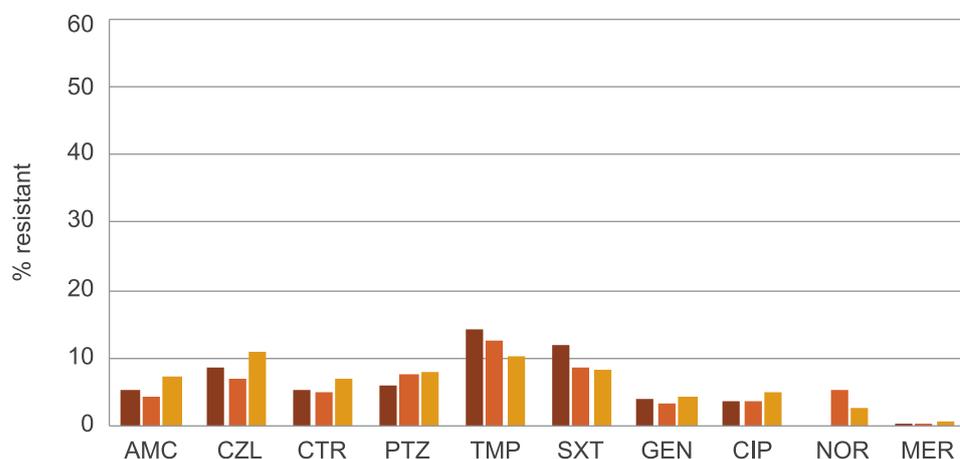


	AMP	AMC	CZL	CTR	PTZ	TMP	SXT	GEN	CIP	NOR	MER
Public hospitals (n = 66,120)	47.3	14.5	17.7	7.3	5.0	24.1	22.7	5.5	8.3	11.2	0.0
Private hospitals (n = 21,504)	42.4	6.7	22.9	9.1	6.3	20.6	24.9	5.0	10.8	7.5	0.1
Community (n = 60,089)	40.4	6.2	18.3	–	–	20.9	19.9	5.7	–	4.6	–
Aged care home (n = 3,282)	44.8	8.9	29.7	–	–	26.6	48.6	4.0	–	11.3	–

– = not available (either not tested or tested against an inadequate number of isolates); AMC = amoxicillin-clavulanate; AMP = ampicillin; CIP= ciprofloxacin; CTR = ceftriaxone; CZL = cefazolin; GEN = gentamicin; MER = meropenem; NOR = norfloxacin; PTZ = piperacillin-tazobactam; SXT = trimethoprim-sulfamethoxazole; TMP = trimethoprim

Sources: AGAR, National Passive AMR Surveillance System (OrgTRx) (public hospitals); AGAR and SNP (private hospitals); OrgTRx (SA) and SNP (community and aged care homes)

Figure 4.6: *Klebsiella pneumoniae* resistance, by specimen source, 2015

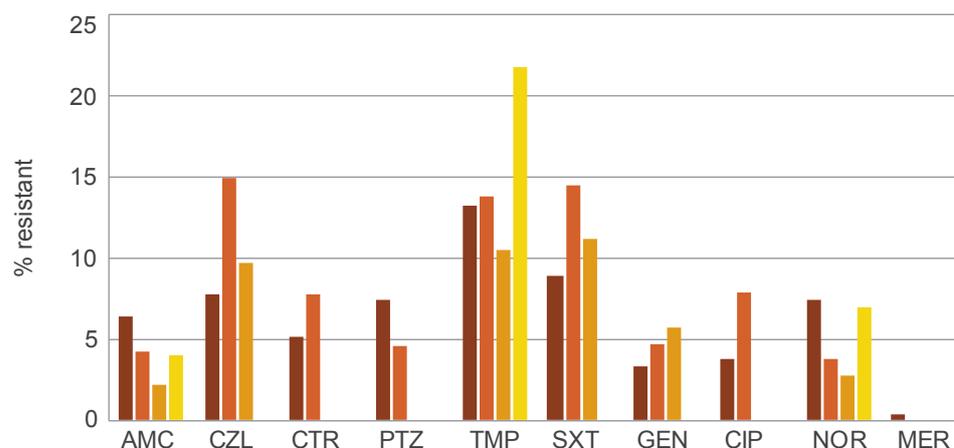


	AMC	CZL	CTR	PTZ	TMP	SXT	GEN	CIP	NOR	MER
Blood (n = 1,996)	5.3	8.7	5.1	6.0	14.1	11.8	4.1	3.7	–	0.3
Urine (n = 15,483)	4.4	6.8	5.0	7.6	12.6	8.6	3.2	3.7	5.1	0.3
Other (n = 2,050)	7.3	10.8	7.0	7.7	10.1	8.1	4.2	4.8	2.7	0.5

– = not available (either not tested or tested against an inadequate number of isolates); AMC = amoxicillin-clavulanate; CIP= ciprofloxacin; CTR = ceftriaxone; CZL = cefazolin; GEN = gentamicin; MER = meropenem; NOR = norfloxacin; PTZ = piperacillin-tazobactam; SXT = trimethoprim-sulfamethoxazole; TMP = trimethoprim

Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

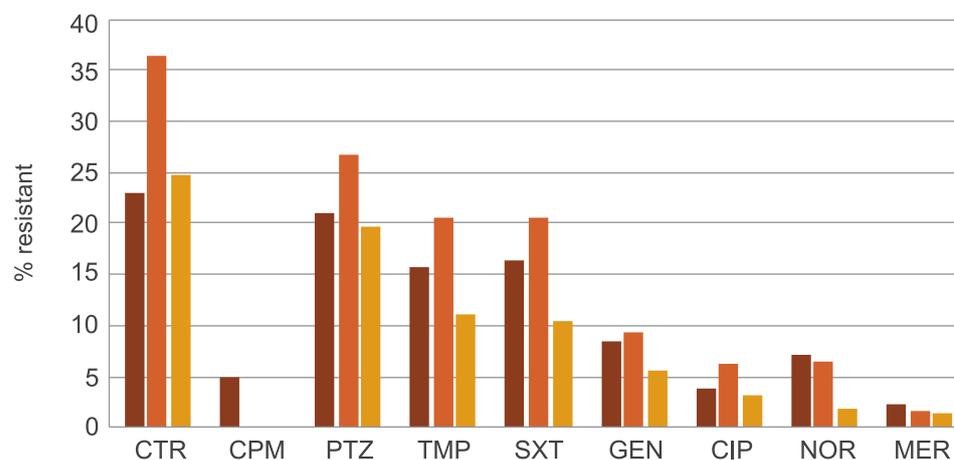
Figure 4.7: *Klebsiella pneumoniae* resistance, by clinical setting, 2015



	AMC	CZL	CTR	PTZ	TMP	SXT	GEN	CIP	NOR	MER
Public hospitals (n = 10,743)	6.3	7.7	5.2	7.4	13.2	8.9	3.3	3.7	7.4	0.4
Private hospitals (n = 1,854)	4.3	14.9	7.8	4.5	13.7	14.4	4.7	7.8	3.8	0.0
Community (n = 6,056)	2.1	9.7	–	–	10.4	11.2	5.6	–	2.8	–
Aged care home (n = 502)	4.0	–	–	–	21.7	–	–	–	7.0	–

– = not available (either not tested or tested against an inadequate number of isolates); AMC = amoxicillin-clavulanate; CIP= ciprofloxacin; CTR = ceftriaxone; CZL = cefazolin; GEN = gentamicin; MER = meropenem; NOR = norfloxacin; PTZ = piperacillin-tazobactam; SXT = trimethoprim-sulfamethoxazole; TMP = trimethoprim
 Sources: AGAR and National Passive AMR Surveillance System (OrgTRx) (public hospitals); AGAR, OrgTRx (SA) and SNP (private hospitals); OrgTRx (SA) and SNP (community and aged care homes)

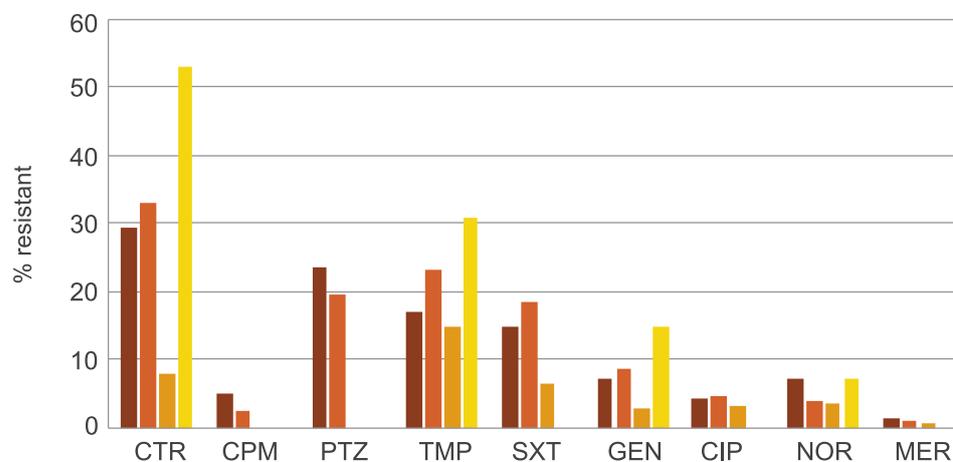
Figure 4.8: *Enterobacter cloacae* complex resistance, by specimen source, 2015



	CTR	CPM	PTZ	TMP	SXT	GEN	CIP	NOR	MER
Blood (n = 553)	22.8	4.9	20.9	15.6	16.3	8.3	3.6	7.0	2.2
Urine (n = 4,227)	36.2	–	26.6	20.4	20.4	9.2	6.2	6.4	1.6
Other (n = 2,279)	24.7	–	19.5	10.9	10.2	5.4	3.1	1.7	1.4

– = not available (either not tested or tested against an inadequate number of isolates); CIP = ciprofloxacin; CPM = ceftazidime; CTR = ceftriaxone; GEN = gentamicin; MER = meropenem; NOR = norfloxacin; PTZ = piperacillin-tazobactam; SXT = trimethoprim-sulfamethoxazole; TMP = trimethoprim
 Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

Figure 4.9: *Enterobacter cloacae* complex resistance, by clinical setting, 2015



Public hospitals (n = 4,172)	29.4	5.3	23.8	17.1	15.1	7.2	4.4	7.4	1.6
Private hospitals (n = 889)	33.2	2.4	19.5	23.5	18.4	8.9	4.9	3.9	1.2
Community (n = 1,512)	8.2	–	–	14.8	6.5	3.0	3.2	3.5	0.6
Aged care home (n = 182)	53.2	–	–	30.8	–	15.0	–	7.1	–

– = not available (either not tested or tested against an inadequate number of isolates); CIP = ciprofloxacin; CPM = cefepime; CTR = ceftriaxone; CPM = cefepime; GEN = gentamicin; MER = meropenem; NOR = norfloxacin; PTZ = piperacillin-tazobactam; SXT = trimethoprim-sulfamethoxazole; TMP = trimethoprim

Sources: AGAR and National Passive AMR Surveillance System (OrgTRx) (public hospitals); AGAR, OrgTRx (SA) and SNP (private hospitals); OrgTRx (SA) and SNP (community and aged care homes)

Key findings: states and territories

Data on resistance were analysed by AURA from blood culture isolates across the states and territories through the AGAR program. Tables 4.4–4.6 show the resistance rates to all antimicrobials tested. There were some notable differences between the states and territories in the prevalence of some important resistances.

For *E. coli*, resistance to ceftriaxone ranged from 0.0% in Tasmania to 15.2% in New South Wales; resistance to gentamicin ranged from 2.5% in Tasmania to 9.4% in New South Wales; and resistance to ciprofloxacin ranged from 3.8% in Tasmania to 16.9% in New South Wales. Resistance to fluoroquinolones is increasing in *E. coli*, despite no increase in the use of this antibiotic class in the community (where access is restricted) or in hospitals.

For *K. pneumoniae*, resistance to ceftriaxone ranged from 2.9% in the Australian Capital Territory to 10.2% in Victoria; resistance to

gentamicin ranged from 2.7% in Western Australia to 10.6% in the Northern Territory; and resistance to ciprofloxacin ranged from 2.1% in the Northern Territory to 5.7% in the Australian Capital Territory.

For *E. cloacae* complex, resistance to gentamicin ranged from 0.0% in South Australia, Western Australia and the Australian Capital Territory to 12.9% in New South Wales; and resistance to ciprofloxacin ranged from 0.0% in Western Australia, South Australia, Tasmania, the Australian Capital Territory and the Northern Territory to 5.9% in New South Wales.

Resistance to fluoroquinolones is increasing in E. coli, despite no increase in the use of this antibiotic class in the community (where access is restricted) or in hospitals.



Table 4.4: Percentage of *Escherichia coli* resistance, by state and territory of testing (blood culture isolates), 2015

Antimicrobial	NSW (n = 1,107)	Vic (n = 727)	Qld (n = 691)	SA (n = 454)	WA (n = 650)	Tas (n = 79)	NT (n = 137)	ACT (n = 149)	Australia, % (n)
Amikacin	0.1	0.1	0.0	0.0	0.2	0.0	0.7	0.7	0.1 (3,994)
Amoxicillin-clavulanate	9.1	10.6	7.8	6.2	8.6	12.7	13.1	3.4	8.7 (3,995)
Ampicillin	57.6	59.8	53.1	45.5	55.7	45.6	59.9	51.0	55.1 (3,992)
Cefazolin	25.1	24.7	20.1	18.1	19.0	10.2*	21.9	18.8	21.8 (3,764)
Cefepime	8.4	5.0	1.3	4.6	3.5	0.0	1.5	4.7	4.8 (3,994)
Ceftazidime	9.9	6.3	3.2	4.4	4.8	0.0	3.6	5.4	6.1 (3,994)
Ceftriaxone	15.2	12.1	6.1	7.3	9.4	0.0	8.8	10.7	10.5 (3,994)
Ciprofloxacin	16.9	13.3	8.1	8.6	14.5	3.8	8.8	10.1	12.6 (3,994)
Gentamicin	9.4	6.9	6.7	7.3	9.2	2.5	8.8	4.7	7.9 (3,994)
Meropenem	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0 (3,993)
Nitrofurantoin	1.0	2.2	0.7	1.3	1.5	0.0	0.0	1.3	1.3 (3,994)
Norfloxacin	22.9	20.5	14.2	11.5	22.9	10.1	13.9	15.4	18.8 (3,993)
Piperacillin-tazobactam	6.3	7.4	7.5	4.6	5.7	5.1	6.6	3.4	6.3 (3,974)
Ticarcillin-clavulanate	25.3	22.2	19.4	20.9	18.0	13.9	19.7	14.1	21.1 (3,871)
Tobramycin	10.2	9.2	6.8	7.5	10.2	2.5	11.7	4.0	8.8 (3,982)
Trimethoprim	34.8	33.0	30.2	24.4	30.6	15.2	35.0	30.9	31.3 (3,982)
Trimethoprim-sulfamethoxazole	33.0	30.9	28.5	23.0	26.5	15.2	32.8	30.2	29.2 (3,990)

* n = 49

Notes:

1. Resistance was determined using European Committee on Antimicrobial Susceptibility Testing interpretive criteria.

2. Not all antimicrobial agents were reported for all isolates.

Source: AGAR (national)

Table 4.5: Percentage of *Klebsiella pneumoniae* resistance, by state and territory of testing (blood culture isolates), 2015

Antimicrobial	NSW (n = 236)	Vic (n = 177)	Qld (n = 189)	SA (n = 85)	WA (n = 187)	Tas (n = 18)	NT (n = 47)	ACT (n = 35)	Australia, % (n)
Amikacin	0.0	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.1 (974)
Amoxicillin-clavulanate	5.1	5.6	3.7	2.4	2.1	5.6	4.3	8.6	4.2 (974)
Ampicillin	94.9	96.0	92.6	90.6	97.3	100.0	100.0	97.1	95.2 (974)
Cefazolin	10.6	16.7*	9.0	8.2	8.5	11.1 [†]	17.0	8.6	10.9 (916)
Cefepime	3.8	3.4	1.6	2.4	0.5	0.0	2.1	0.0	2.3 (974)
Ceftazidime	6.8	9.6	3.2	2.4	2.1	5.6	2.1	2.9	4.9 (974)
Ceftriaxone	6.8	10.2	3.7	3.5	3.7	5.6	6.4	2.9	5.7 (974)
Ciprofloxacin	5.1	5.6	2.6	2.4	2.7	5.6	2.1	5.7	3.9 (974)
Gentamicin	5.9	4.0	3.2	5.9	2.7	5.6	10.6	2.9	4.5 (974)
Meropenem	0.0	0.6	0.0	1.2	0.0	0.0	0.0	2.9	0.3 (974)
Norfloxacin	14.4	17.5	9.0	7.1	11.2	5.6	4.3	8.6	11.8 (974)
Piperacillin-tazobactam	6.4	7.4	7.1	4.7	4.3	5.6	12.8	5.7	6.4 (966)
Ticarcillin-clavulanate	10.8 [§]	13.0	7.9	10.6	8.0	11.1	8.5	11.4	10.0 (951)
Tobramycin	6.8	6.8	3.8	5.9	3.2	5.6	10.6	2.9	5.5 (969)
Trimethoprim	15.3	19.8	15.2	14.1	11.8	22.2	17.0	31.4	16.1 (969)
Trimethoprim-sulfamethoxazole	12.3	16.4	14.8	9.4	6.4	16.7	14.9	28.6	12.9 (974)

* n = 150

† n = 9

§ n = 213

Notes:

1. Resistance was determined using European Committee on Antimicrobial Susceptibility Testing interpretive criteria.
2. Not all antimicrobial agents were reported for all isolates.

Source: AGAR (national)



Table 4.6: Percentage of *Enterobacter cloacae* complex resistance, by state and territory of testing (blood culture isolates), 2015

Antimicrobial	NSW (n = 85)	Vic (n = 80)	Qld (n = 65)	SA (n = 13)	WA (n = 50)	Tas (n = 14)	NT (n = 9)	ACT (n = 10)	Australia, % (n)
Amikacin	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0 (326)
Amoxicillin-clavulanate	84.7	91.3	92.3	84.6	90.0	78.6	88.9	100.0	89.0 (326)
Ampicillin	87.8	90.0	92.3	76.9	92.0	92.9	88.9	90.0	89.8 (315)
Cefazolin	91.8	98.6	98.5	100.0	100.0	87.5*	88.9	100.0	96.5 (312)
Cefepime	4.7	8.8	4.6	0.0	0.0	0.0	0.0	0.0	4.3 (326)
Ceftazidime	23.5	27.5	23.1	0.0	20.0	28.6	22.2	0.0	22.4 (326)
Ceftriaxone	24.7	30.0	27.7	0.0	22.0	21.4	22.2	10.0	24.5 (326)
Ciprofloxacin	5.9	5.0	3.1	0.0	0.0	0.0	0.0	0.0	3.4 (326)
Gentamicin	12.9	5.0	10.8	0.0	0.0	7.1	11.1	0.0	7.4 (326)
Meropenem	4.7	0.0	4.6	0.0	0.0	0.0	0.0	0.0	2.1 (326)
Norfloxacin	10.6	10.0	9.2	0.0	0.0	0.0	0.0	10.0	7.4 (326)
Piperacillin-tazobactam	14.0 [†]	27.3	18.8	7.7	26.8	18.2	22.2	0.0 [§]	20.6 (277)
Ticarcillin-clavulanate	23.0	31.3	26.2	0.0	22.0	21.4	22.2	0.0	23.8 (315)
Tobramycin	14.1	10.0	12.5	0.0	0.0	7.1	11.1	0.0	9.2 (325)
Trimethoprim	16.5	20.0	18.8	15.4	2.0	21.4	22.2	20.0	16.0 (325)
Trimethoprim-sulfamethoxazole	16.5	18.8	18.5	15.4	2.0	21.4	22.2	20.0	15.6 (326)

* n = 8

† n = 57

§ n = 5

Notes:

1. Resistance was determined using European Committee on Antimicrobial Susceptibility Testing interpretive criteria.

2. Not all antimicrobial agents were reported for all isolates.

Source: AGAR (national)

Additional findings from targeted surveillance

AGAR also captured data on 30-day all-cause mortality (Tables 4.7 and 4.8). Unless otherwise stated, these findings apply to all species of Enterobacteriaceae detected.

Significantly higher 30-day all-cause mortality occurred when the bacteraemia had its onset in the hospital. For *E. coli* and *K. pneumoniae*, the effect of multi-drug resistance on 30-day all-cause mortality was small, but there was a noticeable effect on mortality with *E. cloacae* complex. This may be due to the smaller range of effective antimicrobials that remain available for treatment of infections cause by *E. cloacae* complex.

For E. coli and K. pneumoniae, the effect of multi-drug resistance on 30-day all-cause mortality was small, but there was a noticeable effect on mortality with E. cloacae complex.

Data for gram-negative bacteria can be found on the AURA and AGAR websites.

Table 4.7: Onset setting and 30-day all-cause mortality for the 12 most commonly isolated gram-negative species (blood culture isolates), 2015

Species	Community, <i>n</i>	Community mortality, % (<i>n</i>)	Hospital, <i>n</i>	Hospital mortality, % (<i>n</i>)	Total, <i>n</i>	Total mortality, % (<i>n</i>)
<i>Escherichia coli</i>	2,009	8.4 (169)	422	21.3 (90)	2,431	10.7 (259)
<i>Klebsiella pneumoniae</i>	452	12.6 (57)	195	15.4 (30)	647	13.4 (87)
<i>Enterobacter cloacae</i> complex	112	14.6 (16)	117	12.8 (15)	229	13.5 (31)
<i>Klebsiella oxytoca</i>	111	8.1 (9)	44	13.6 (6)	155	9.7 (15)
<i>Proteus mirabilis</i>	111	18.9 (21)	26	38.5 (10)	137	22.6 (31)
<i>Serratia marcescens</i>	60	11.7 (7)	71	19.7 (14)	131	16.0 (21)
<i>Enterobacter aerogenes</i>	42	9.5 (4)	38	18.4 (7)	80	13.8 (11)
<i>Salmonella</i> species (non-typhoidal)	61	3.3 (2)	12	25.0 (3)	73	6.8 (5)
<i>Morganella morganii</i>	35	14.3 (5)	17	29.4 (5)	52	19.2 (10)
<i>Citrobacter koseri</i>	28	7.1 (2)	14	21.4 (3)	42	11.9 (5)
<i>Citrobacter freundii</i>	24	25.0 (6)	7	42.8 (3)	31	29.0 (9)
<i>Salmonella</i> species (typhoidal)	13	0.0 (0)	0	0.0 (0)	13	0.0 (0)
Total (all species)	3,389	10.6 (358)	1,197	18.7 (224)	4,586	14.1 (647)

Source: AGAR (national)

Table 4.8: Onset setting and 30-day all-cause mortality for the three most commonly isolated Enterobacteriaceae species, by multi-drug resistance (blood culture isolates), 2015

Species	Category	Community, <i>n</i>	Community mortality, % (<i>n</i>)	Hospital, <i>n</i>	Hospital mortality, % (<i>n</i>)	Total, <i>n</i>	Total mortality, % (<i>n</i>)
<i>Escherichia coli</i>	Total	1,880	8.6 (162)	392	20.9 (82)	2,272	10.7 (244)
	Non-multidrug resistant	1,475	8.4 (124)	259	20.8 (54)	1,734	10.3 (178)
	Multidrug resistant	405	9.4 (38)	133	21.1 (28)	538	12.3 (66)
<i>Enterobacter cloacae</i> complex	Total	99	12.1 (12)	101	10.9 (11)	200	11.5 (23)
	Non-multidrug resistant	89	9.0 (8)	78	10.3 (8)	167	9.6 (16)
	Multidrug resistant	10	40.0 (4)	23	13.0 (3)	33	21.2 (7)
<i>Klebsiella pneumoniae</i>	Total	431	12.8 (55)	179	16.2 (29)	610	13.8 (84)
	Non-multidrug resistant	395	12.7 (50)	153	15.7 (24)	548	13.5 (74)
	Multidrug resistant	36	13.9 (5)	26	19.2 (5)	62	16.1 (10)

Note: Multidrug-resistant strains are resistant to three or more antimicrobial classes. Intrinsic resistances were excluded from the definition of multi-drug resistance in *K. pneumoniae* and *E. cloacae*. Cefazolin was excluded from the definition because data on minimum inhibitory concentrations are not recorded by some institutions. The antimicrobials used to define multi-drug resistance were:

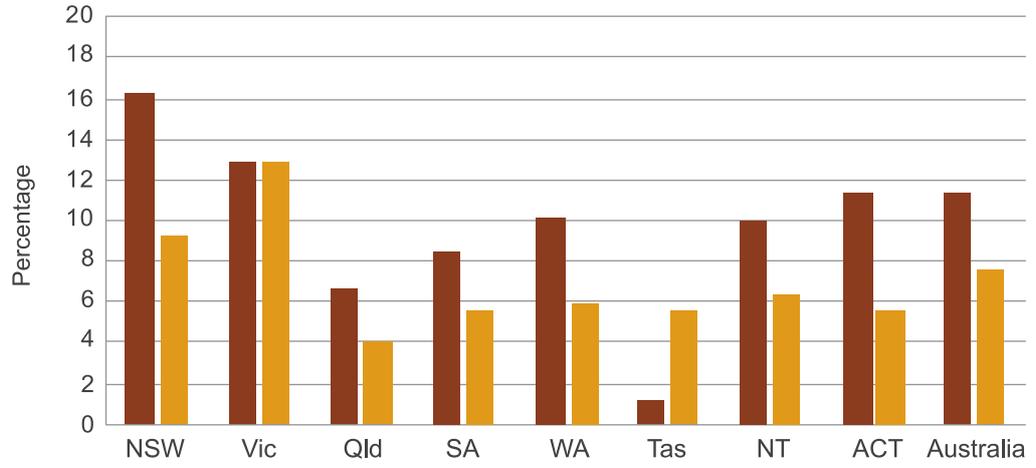
- *E. coli* - ampicillin, amoxicillin-clavulanate, piperacillin-tazobactam, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem
- *K. pneumoniae* - amoxicillin-clavulanate, piperacillin-tazobactam, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem
- *E. cloacae* - piperacillin-tazobactam, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem.

Source: AGAR (national)

AURA defines multidrug-resistant organisms as those that have acquired resistance to three or more antimicrobial classes, where all agents have been tested.

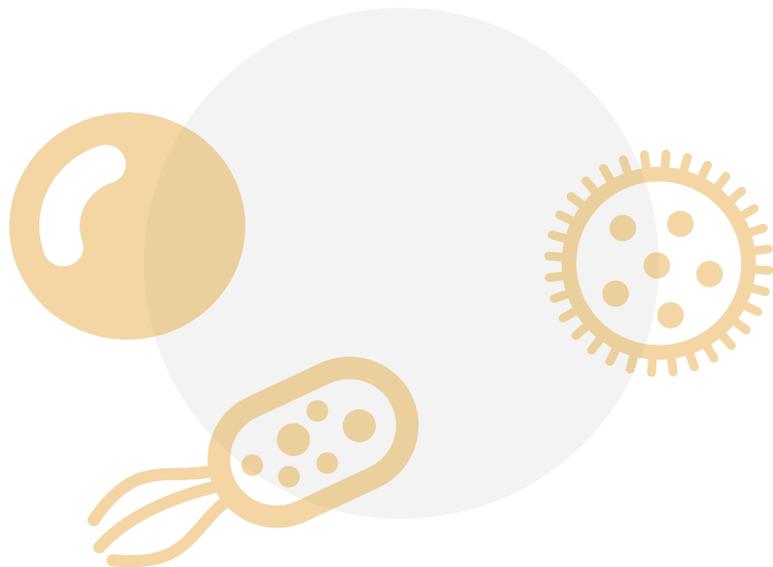
E. coli and *K. pneumoniae* strains that are resistant to ceftriaxone and/or ceftazidime (MIC >1 mg/L; ESBL phenotype), and their variation across states and territories are shown in Figure 4.10.

Figure 4.10: Percentage of *Escherichia coli* and *Klebsiella pneumoniae* with extended-spectrum β-lactamase phenotype, by state and territory, 2015



■ <i>E. coli</i> (n = 4,006)	16.3	13	6.7	8.6	10.3	1.3	10.1	11.4	11.5
■ <i>K. pneumoniae</i> (n = 977)	9.3	13	4.2	5.7	5.9	5.6	6.4	5.7	7.7

Note: The extended-spectrum β-lactamase phenotype has a minimum inhibitory concentration >1 mg/mL for ceftriaxone or ceftazidime.
Source: AGAR (public and private hospitals)



● From information to action

Using antibiograms to adapt local empirical prescribing guidelines

A rural Queensland Hospital and Health Service district reviews its local antimicrobial susceptibility data every year to update local empirical antimicrobial prescribing guidelines.

This district covers more than 158,000 km² of rural and remote north Queensland. It includes 31 primary healthcare centres, and four hospitals ranging from 10 to 45 beds. The district relies heavily on local prescribing guidelines to ensure appropriate prescribing across the various healthcare settings, most of which do not have on-site pharmacists or full-time on-site medical officers.

The district antibiogram was collated using data from the National Passive AMR Surveillance System (OrgTRx). The local antimicrobial stewardship (AMS) governance team used the data to inform antimicrobial guidelines and detect changes in local susceptibility patterns.

In 2016, review of the district antibiogram showed a significant ($P < 0.05$) decrease in susceptibility to cefalexin/cefazolin among *Escherichia coli* isolates from urine samples compared with 2015 (Figure A). This decrease in susceptibility meant that these agents could no longer be considered as first-line therapy for cystitis, particularly where other reliable agents were available.

The local AMS governance team used the antibiogram data to remove cefalexin/cefazolin as first-line treatment for urinary tract infections from their local prescribing guidelines. The use of local antimicrobial susceptibility data also facilitated continued adaptation of national empirical guidelines into local prescribing recommendations, to ensure that the recommendations reflect the unique patient demographics of rural Queensland.

Figure A: Cumulative antibiogram for the district, 2015–16

Organism	Number of isolates		% susceptible to routinely reported antibiotics											
			Ampicillin/amoxicillin		Amoxicillin-clavulanate		Cefalexin/cefazolin		Trimethoprim		Nitrofurantoin		Gentamicin	
	2015	2016	2015	2016	2015	2016	2015	2016	2015	2016	2015	2016	2015	2016
<i>Escherichia coli</i>	731	638	52	51	84	87	74	69	72	72	99	100	96	95
<i>Klebsiella pneumoniae</i>	124	118			93	95	82	90	86	85	53	55	97	100

Susceptibility categories

■ <70% of isolates sensitive ■ 70–90% of isolates sensitive ■ >90% of isolates sensitive

■ Not tested, not clinically effective or intrinsically resistant

4.4 *Enterococcus* species

This section describes the health impact, treatment, types and impact of resistance, and key findings for resistance rates in *Enterococcus* species.

Health impact

Enterococcus species are opportunistic pathogens that cause a range of infections in patients whose physical barriers are compromised through surgery or invasive devices. They rarely cause disease in healthy people, but may cause infections in vulnerable patients, such as people who are very elderly or immunosuppressed.

They are a cause of urinary tract infection in patients with catheters or structural abnormalities, and are associated with other

intestinal organisms in many intra-abdominal infections, especially those of the biliary tract. These infections can be complicated by septicaemia. Enterococci are also a less common, but important, cause of endocarditis. The most common clinical syndromes associated with enterococcal septicaemia were biliary and urinary tract infections (Table 4.9).

Treatment

Enterococci are naturally resistant to a range of common antimicrobial classes, including anti-staphylococcal penicillins, cephalosporins, macrolides and lincosamides. Amoxicillin administered orally is the most common treatment for minor infections. More serious infections are treated with intravenous ampicillin or amoxicillin; for endocarditis, one of these agents is often combined with low-dose

Table 4.9: Principal clinical manifestations of infection with *Enterococcus* species (blood culture isolates), 2015

Principal clinical manifestation	Male	Female	Total
Biliary tract infection (including cholangitis)	99	62	161
Urinary tract infection	124	33	157
Intra-abdominal infection other than biliary tract	84	51	135
No focus (setting known; e.g. in febrile neutropenia)*	77	39	116
Febrile neutropenia*	50	31	81
No focus (setting not known)*	4	2	6
Device-related infection without metastatic focus	58	38	96
Other clinical syndrome	39	21	60
Endocarditis, left-sided	42	16	58
Skin and skin structure infection	24	12	36
Osteomyelitis/septic arthritis	14	6	20
Endocarditis, right-sided	6	6	12
Device-related infection with metastatic focus	6	4	10
Pneumonia/empyema	1	0	1
Total	628	321	949

* These principal clinical manifestations reflect the variation in reporting by contributors.
Source: AGAR (national)

gentamicin. Vancomycin is used instead of ampicillin/amoxicillin for serious infections in patients who are allergic to penicillins.

Types and impact of resistance

Ampicillin resistance has emerged worldwide at quite high levels in *E. faecium* during the past 20 years, including in Australia, increasing the use of vancomycin for treatment. More recently, vancomycin-resistant enterococci (VRE) have also emerged, most notably in *E. faecium*, but also in *E. faecalis*. The gene complexes responsible are of two main types, *vanA* and *vanB*. In Australia, unlike in most other countries, VRE have been dominated by the *vanB*, rather than the *vanA*, genotype. VRE require treatment with agents that are usually reserved, such as teicoplanin or daptomycin.

Key findings: national

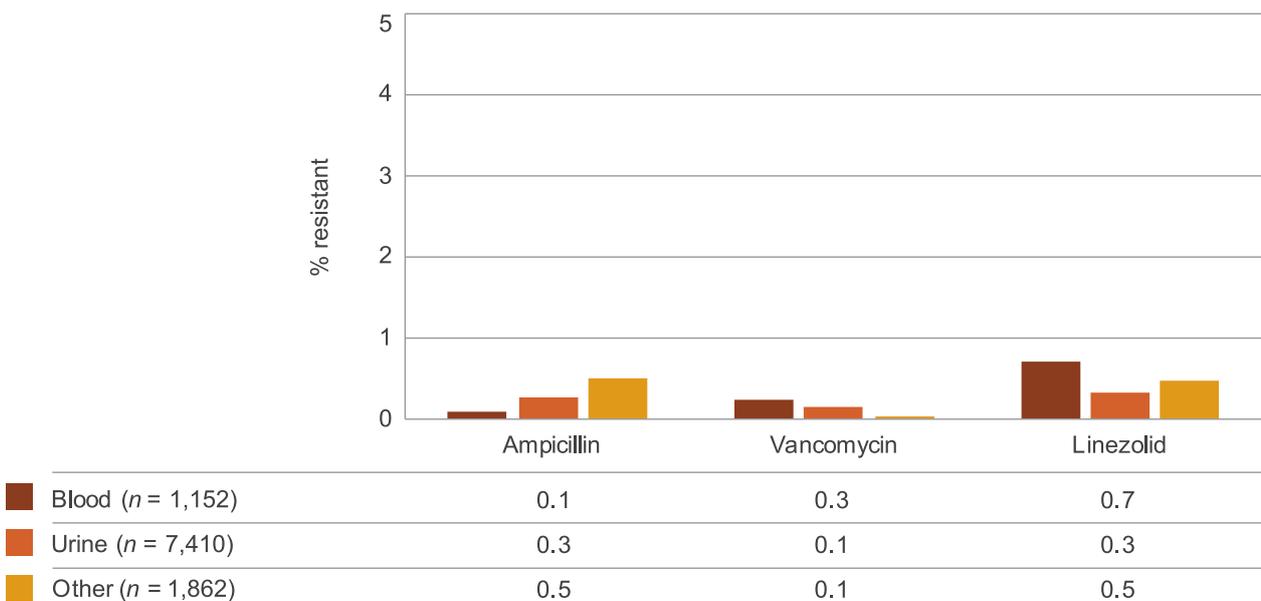
Rates of resistance to key antimicrobials in *E. faecalis* were very low – in 2015, less than 1% of isolates from blood ($n = 1,152$), urine ($n = 7,410$)

and other sites ($n = 1,862$) were resistant to ampicillin, vancomycin or linezolid (Figure 4.11). Rates of resistance showed some differences by clinical setting (Figure 4.12).

Rates of resistance to key antimicrobials in E. faecalis were very low, but rates of resistance in E. faecium to ampicillin and vancomycin were high.

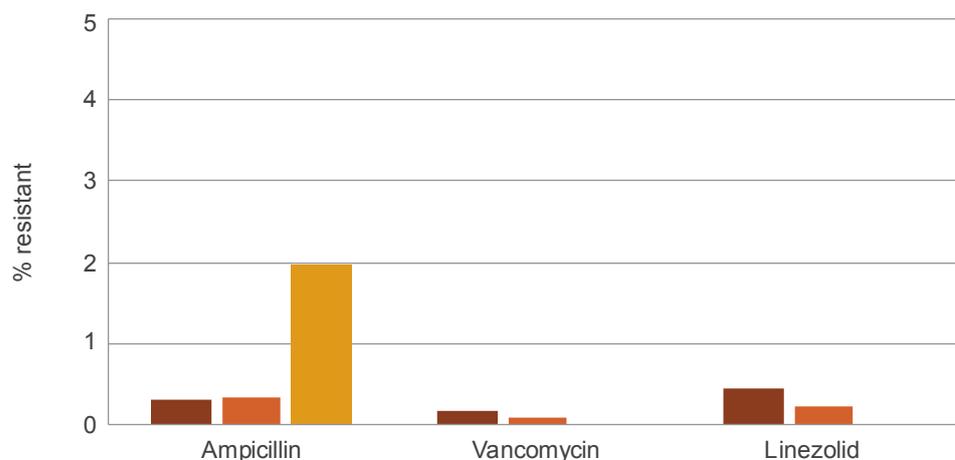
In contrast, rates of resistance in *E. faecium* to ampicillin and vancomycin were high (Figures 4.13 and 4.14). Linezolid resistance was rare. Specimen source did not substantially influence rates of resistance (Figure 4.13). There was some variation in the rates of vancomycin resistance in *E. faecium*, depending on the setting (Figure 4.14). Rates were higher in the private hospital and community sectors than in the public hospital sector. This may have been a sampling issue, given that most of the community and private hospital data came from Queensland and South Australia.

Figure 4.11: *Enterococcus faecalis* resistance, by specimen source, 2015



Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

Figure 4.12: *Enterococcus faecalis* resistance, by clinical setting, 2015

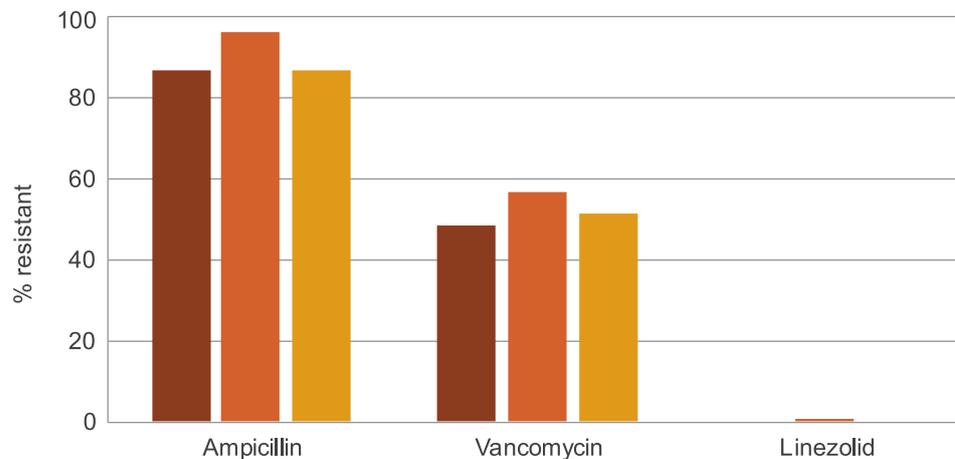


Public hospitals (<i>n</i> = 8,997)	0.3	0.2	0.4
Private hospitals (<i>n</i> = 1,479)	0.3	0.1	0.2
Community (<i>n</i> = 54)	2.0	–	0.0

– = not available (either not tested or tested against an inadequate number of isolates)

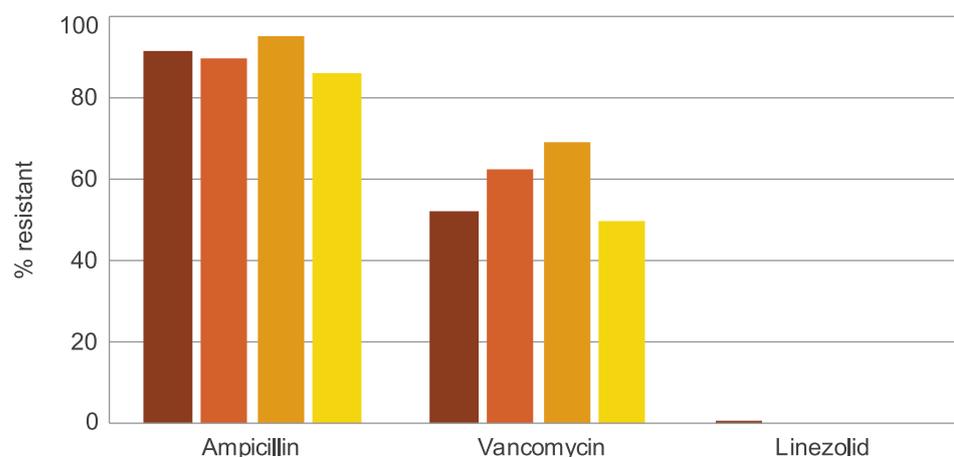
Sources: AGAR and National Passive AMR Surveillance System (OrgTRx) (public hospitals); AGAR, OrgTRx (SA) and SNP (private hospitals); OrgTRx (SA) and SNP (community)

Figure 4.13: *Enterococcus faecium* resistance, by specimen source, 2015



Blood (<i>n</i> = 557)	86.3	48.7	0.0
Urine (<i>n</i> = 1,289)	95.9	56.8	0.4
Other (<i>n</i> = 671)	86.3	51.6	0.0

Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

Figure 4.14: *Enterococcus faecium* resistance, by clinical setting, 2015

Clinical Setting	Ampicillin	Vancomycin	Linezolid
Public hospitals (n = 2,205)	91.4	52.4	0.2
Private hospitals (n = 186)	90.0	62.4	0.0
Community (n = 82)	95.1	69.4	–
Aged care home (n = 51)	86.3	50.0	–

– = not available (either not tested or tested against an inadequate number of isolates)

Sources: AGAR and National Passive AMR Surveillance System (OrgTRx) (public hospitals); AGAR, OrgTRx (SA) and SNP (private hospitals); OrgTRx (SA) and SNP (community and aged care homes)

Key findings: states and territories

The percentages of *Enterococcus* species that were resistant to key antimicrobials are shown in Tables 4.10 and 4.11.

Vancomycin-resistant *E. faecium* is the main AMR issue for *Enterococcus* species. The main type of vancomycin-resistant *E. faecium* circulating in Australia is of the *vanB* type (Figure 4.15). In New South Wales and the Australian Capital Territory, the *vanA* type is now predominant in blood culture isolates.

Additional findings from targeted surveillance

Data from AGAR are available for 30-day all-cause mortality. The all-cause mortality at 30 days was significantly higher for *E. faecium* infections than for *E. faecalis* infections, possibly as a result of greater comorbidities in patients with *E. faecium* infections. Vancomycin resistance in *E. faecalis* appeared to have an even greater association with 30-day mortality (Table 4.12).

The all-cause mortality at 30 days was significantly higher for E. faecium infections than for E. faecalis infections, and vancomycin resistance in E. faecalis appeared to have an even greater association with 30-day mortality.

Vancomycin-resistant enterococci were typed using multilocus sequence typing. Different sequence types had established in different states and territories (although Tasmania aligned with Victoria), consistent with rapid local or regional spread rather than national spread (Figure 4.16).

Full data from AGAR surveys of *Enterococcus* species can be found on the AGAR website.

Table 4.10: Percentage of *Enterococcus faecium* resistance, by state and territory of testing (blood culture isolates), 2015

Antimicrobial	NSW (n = 115)	Vic (n = 120)	Qld (n = 30)	SA (n = 44)	WA (n = 53)	Tas (n = 8)	NT (n = 8)	ACT (n = 22)	Australia, % (n)
Ampicillin	85.2	88.3	83.3	93.2	79.2	50.0	87.5	95.5	86.0 (400)
Ciprofloxacin	64.9	90.0	82.1	11.1*	79.2	100.0	87.5	95.5	74.8 (373)
Linezolid	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0 (400)
Trimethoprim- sulfamethoxazole	47.8	83.9 [†]	70.0	45.5	62.3	100.0	75.0	59.1	59.6 (327)
Vancomycin	51.7	63.3	61.3	52.3	11.3	12.5	75.0	50.0	50.2 (402)

* n = 27

† n = 56

Notes:

1. Resistance was determined using European Committee on Antimicrobial Susceptibility Testing interpretive criteria.
2. Not all antimicrobial agents were reported for all isolates.

Source: AGAR (national)

Table 4.11: Percentage of *Enterococcus faecalis* resistance, by state and territory of testing (blood culture isolates), 2015

Antimicrobial	NSW (n = 150)	Vic (n = 110)	Qld (n = 95)	SA (n = 58)	WA (n = 91)	Tas (n = 12)	NT (n = 10)	ACT (n = 35)	Australia, % (n)
Ampicillin	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0 (561)
Ciprofloxacin	8.7	15.5	9.6*	7.0 [†]	8.8	-	30.0	14.3	10.9 (521)
Linezolid	0.0	0.0	1.1	0.0	0.0	0.0	0.0	0.0	0.2 (561)
Trimethoprim- sulfamethoxazole	16.8	20.9 [§]	24.2	20.7	15.4	-	50.0	22.9	20.0 (505)
Vancomycin	1.3	0.9	0.0	0.0	0.0	8.3	0.0	0.0	0.7 (561)

- = no data available

* n = 83

† n = 43

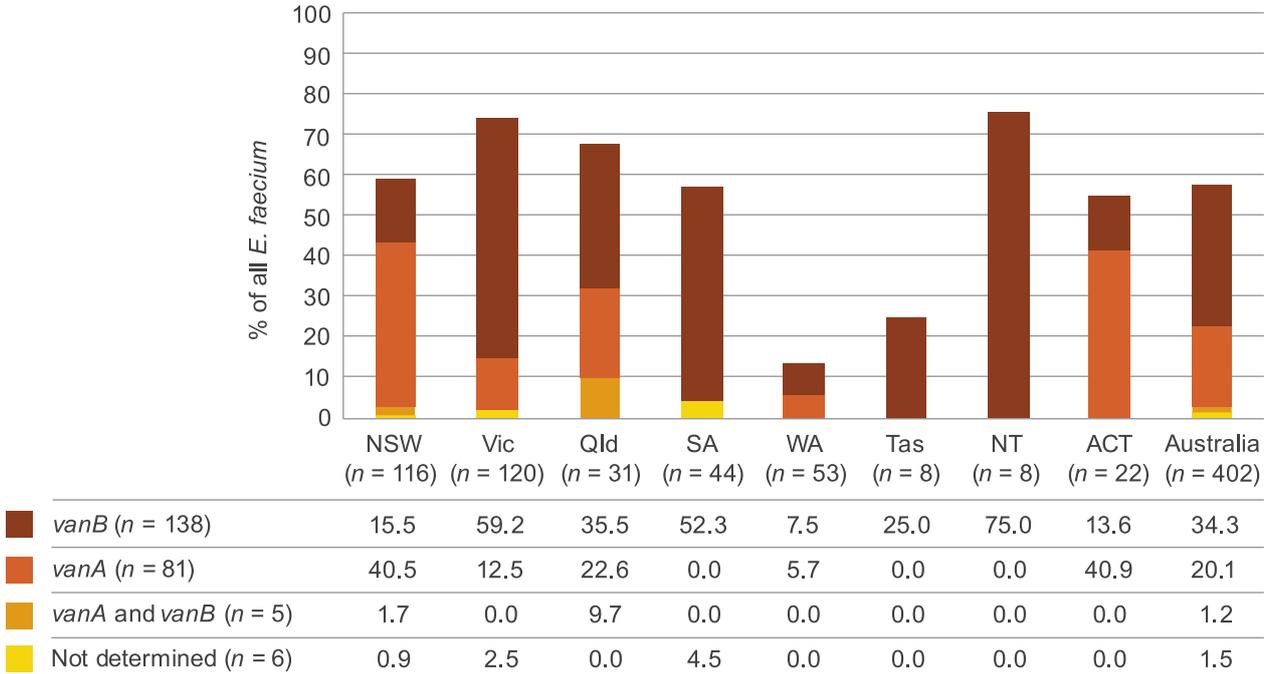
§ n = 67

Notes:

1. Resistance was determined using European Committee on Antimicrobial Susceptibility Testing interpretive criteria.
2. Not all antimicrobial agents were reported for all isolates.

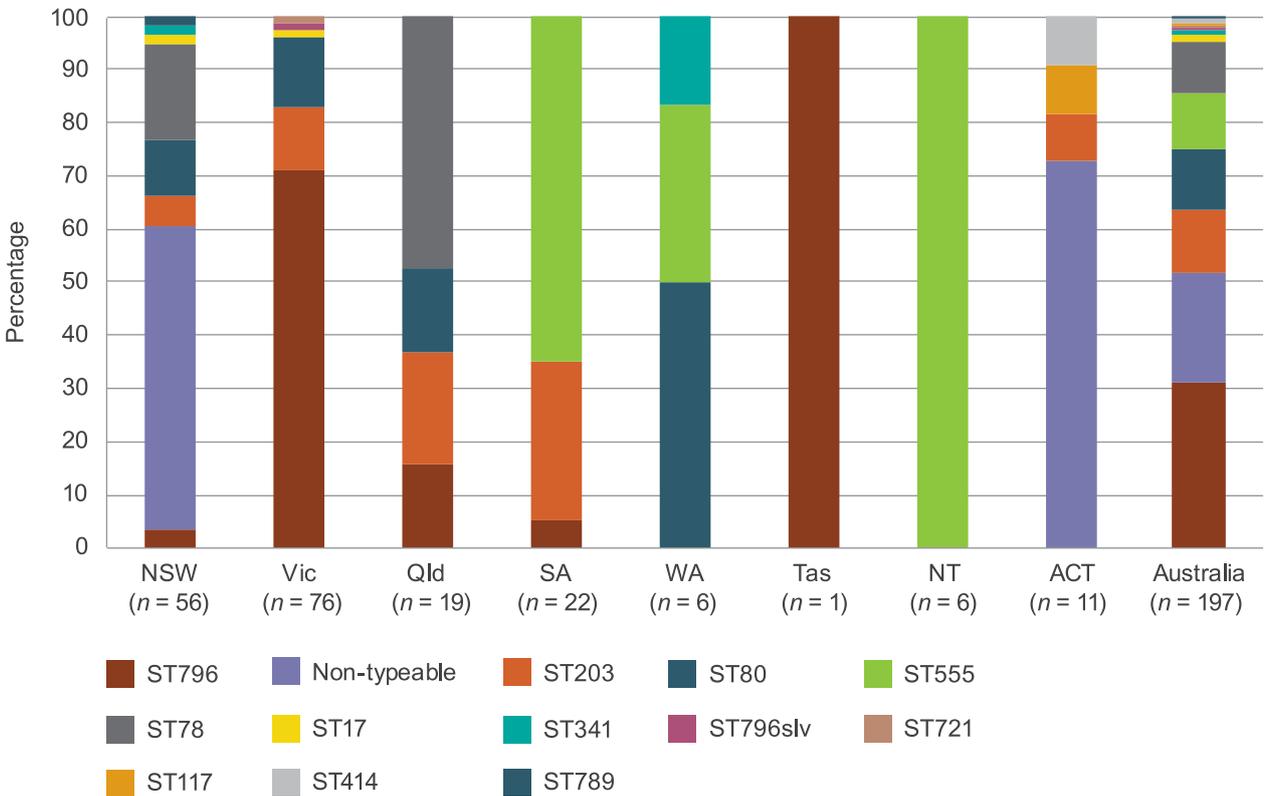
Source: AGAR (national)

Figure 4.15: Vancomycin-resistant *Enterococcus faecium* genotype, by state or territory of testing (blood culture isolates), 2015



Source: AGAR (national)

Figure 4.16: Distribution of vancomycin-resistant *Enterococcus faecium* sequence types, by state or territory of testing (blood culture isolates), 2015



Source: AGAR (national)

Table 4.12: Onset setting and 30-day all-cause mortality for infections with *Enterococcus* (blood culture isolates), 2015

Species	Community, <i>n</i>	Community mortality, % (<i>n</i>)	Hospital, <i>n</i>	Hospital mortality, % (<i>n</i>)	Total, <i>n</i>	Total mortality, % (<i>n</i>)
<i>Enterococcus faecalis</i>	311	16.1 (50)	166	15.1 (25)	477	15.7 (75)
<i>Enterococcus faecium</i>	97	24.7 (24)	275	27.6 (76)	372	26.9 (100)
Vancomycin-susceptible <i>E. faecium</i>	61	21.3 (13)	121	25.6 (31)	182	24.2 (44)
Vancomycin-resistant <i>E. faecium</i>	36	30.6 (11)	154	29.2 (45)	190	29.5 (56)

Source: AGAR (national)

4.5 *Mycobacterium tuberculosis*

This section describes the health impact, treatment, types and impact of resistance, and key findings for resistance rates in *M. tuberculosis*.

Health impact

M. tuberculosis is the bacterium that causes tuberculosis, an infection that has a range of clinical manifestations, but most commonly presents as lung disease. Once acquired, *M. tuberculosis* can remain quiescent in the body for many years (even decades) as latent tuberculosis. When the body’s defences wane, it reactivates and causes active disease. Tuberculosis is a significant public health issue in many countries. Australia is fortunate in having one of the lowest rates of tuberculosis in the world; however, continued vigilance is required to maintain or improve this low rate. About 85% of all notified cases in Australia are found in people born overseas, who have mostly migrated from high-prevalence countries.

Treatment

M. tuberculosis is not susceptible to most conventional antibacterial agents. Instead, it requires treatment with specially designed antimycobacterial agents. Four of these

– isoniazid, rifampicin, ethambutol and pyrazinamide – are the first-line agents and comprise the standard oral treatment regimen for tuberculosis caused by fully susceptible strains. When the strain is susceptible, isoniazid is considered the mainstay of therapy. Combinations of antimycobacterial agents are always required for treatment because resistance to any of them can emerge during treatment. Treatment is required for a minimum of six months.

Types and impact of resistance

Because such a high proportion of Australian cases occur in people born overseas, changes in antimicrobial susceptibility observed in Australia reflect patterns of resistance in these other countries. The most common forms of resistance worldwide are resistance to isoniazid and rifampicin. When strains are resistant to one or both of these agents, additional antimycobacterial agents are added to, or substituted into, the treatment combination. For most of these additional agents, side effects are more likely or more severe. Longer courses of treatment are needed for resistant strains.

Strains that are resistant to isoniazid and rifampicin, with or without resistance to the other two first-line agents, are considered to be multidrug-resistant tuberculosis (MDR-TB). If these strains are also resistant to fluoroquinolones and at least one injectable agent (amikacin,

capreomycin, kanamycin), they are considered to be extremely drug-resistant tuberculosis (XDR-TB). Treatment success is significantly lower, and costs are significantly higher, for MDR-TB, and even more so for XDR-TB.

Treatment success is significantly lower, and costs are significantly higher, for MDR-TB, and even more so for XDR-TB.

Key findings: national

In 2015, 1,244 cases of tuberculosis were notified nationally (5.3 cases per 100,000 population). Of these cases, 968 had positive laboratory cultures and susceptibility test results available. Overall rates of resistance to the four first-line agents and selected additional agents are shown in Figure 4.17.

Key findings: states and territories

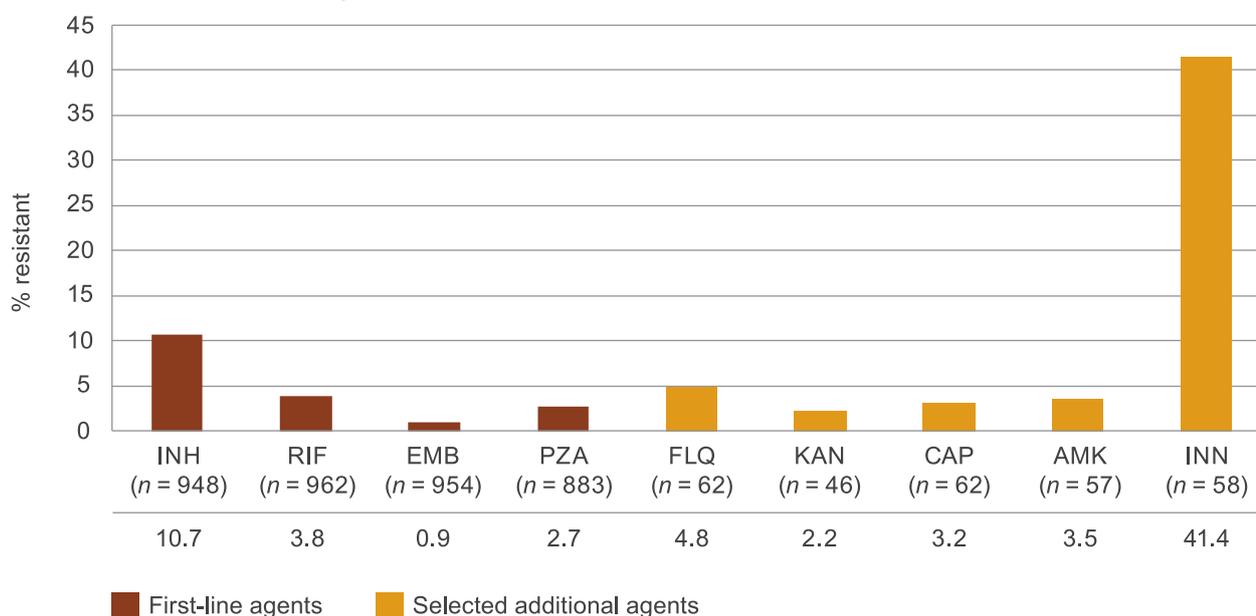
There was some variation in resistance rates to first-line agents across the states and territories (Figure 4.18).

National trends

Overall, rates of resistance have not changed significantly during the past decade. There has been a small trend upwards in the percentage of MDR-TB strains (Figure 4.19). XDR-TB strains have remained rare (2 of 1,255 strains tested in 2015).

Detailed reports of susceptibility data for *M. tuberculosis* from 1996 onwards can be found on the Australian Government Department of Health website. Guidelines for Australian mycobacteriology laboratories have been published in *Communicable Diseases Intelligence*.

Figure 4.17: *Mycobacterium tuberculosis* resistance to individual first-line agents and selected additional agents, 2015



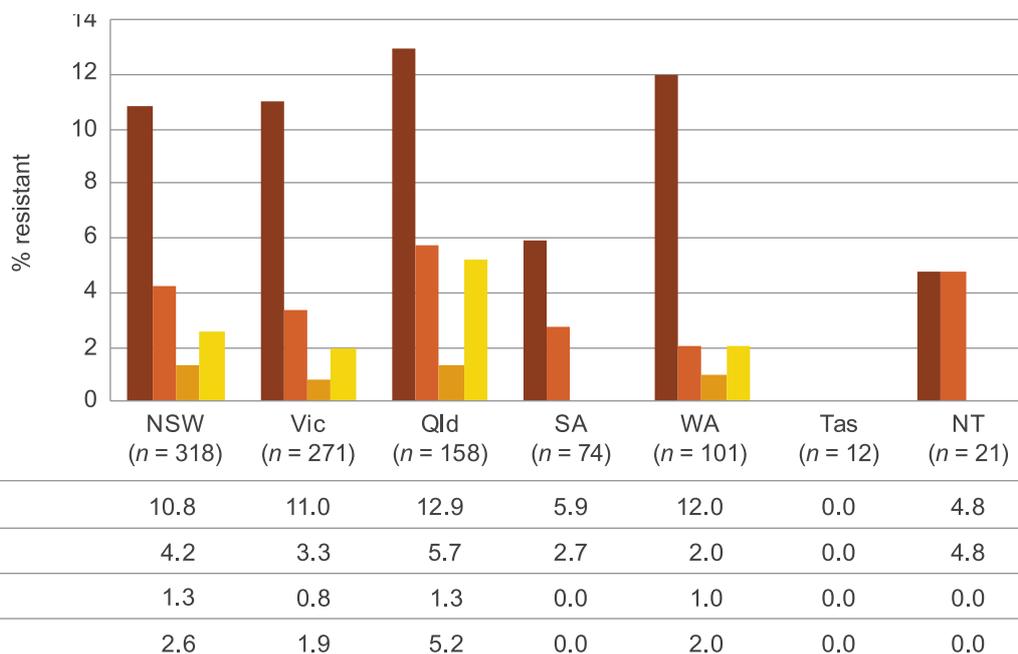
AMI = amikacin; CAP = capreomycin; EMB = ethambutol; FLQ = fluoroquinolones; INH = isoniazid; INN = ethionamide; KAN = kanamycin; PZA = pyrazinamide; RIF = rifampicin

Notes:

1. First-line agents (dark columns) reported against (almost) all strains: isoniazid, rifampicin, ethambutol and pyrazinamide; selected additional agents (light columns) tested against isolates with resistance to first-line agents or from patients with severe adverse reactions to first-line agents.
2. Fluoroquinolones tested were ciprofloxacin, ofloxacin, moxifloxacin or levofloxacin.

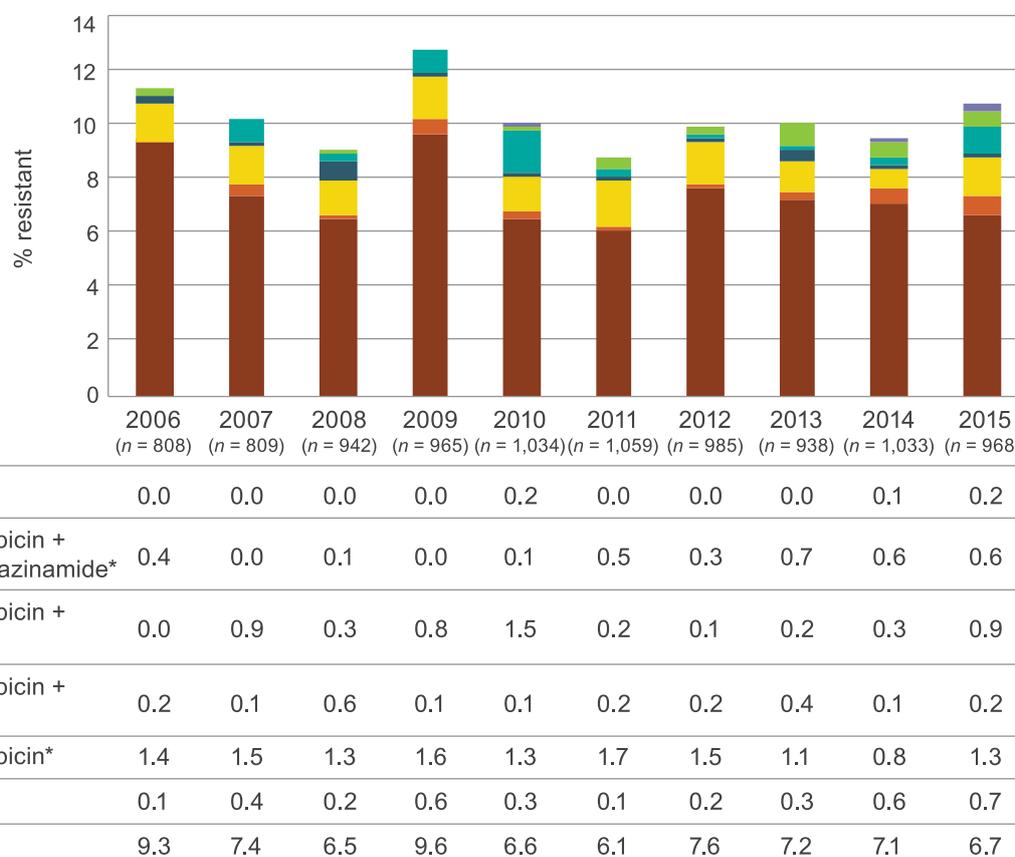
Source: NNDSS (national)

Figure 4.18: *Mycobacterium tuberculosis* resistance to first-line agents, by state and territory, 2015



Source: NNDSS (national)

Figure 4.19: Ten-year trends in resistance and multidrug-resistance patterns in *Mycobacterium tuberculosis*



XDR-TB = extremely drug-resistant tuberculosis

* Multidrug-resistant tuberculosis strains

Source: NNDSS (public and private hospitals and health services)

4.6 *Neisseria gonorrhoeae*

This section describes the health impact, treatment, types and impact of resistance, and key findings for resistance rates in *N. gonorrhoeae*.

Health impact

N. gonorrhoeae causes gonorrhoea, an infection that is largely sexually transmitted, and most commonly manifests as urethritis in men and cervicitis in women. Many infections in women are asymptomatic, but, in some women, the infection ascends to the uterus and fallopian tubes, and can cause infertility if not treated promptly. Women who become infected in late pregnancy can spread the infection to the newborn at the time of delivery. With the advent of nucleic acid testing for gonococcal infection, most cases are now diagnosed using these techniques, and specimens for culture are not collected. Only a minority of cases undergo susceptibility testing, which depends on obtaining a specimen for culture of the organism.

Treatment

Most gonorrhoea is treated empirically, and treatment does not depend on the results of culture and susceptibility testing. The most important reason is that immediate empirical treatment is the most effective tool for preventing further transmission. Thus, treatment is based on standard treatment protocols, which are guided by the prevalence of resistances determined in national surveillance programs.

Most gonorrhoea is treated empirically, and treatment does not depend on the results of culture and susceptibility testing. This is because immediate empirical treatment is the most effective tool for preventing further transmission.

The most important agent for treating gonorrhoea is the third-generation cephalosporin ceftriaxone. This is effective as a single dose in uncomplicated infections such as urethritis or cervicitis. Ceftriaxone has superseded penicillin and ciprofloxacin for first-line treatment, because resistance to these latter agents has emerged. Azithromycin, an antimicrobial used for many years for the treatment of sexually transmitted infections caused by *Chlamydia trachomatis*, is now considered as a treatment option if treatment with ceftriaxone fails.

Types and impact of resistance

Resistance to ceftriaxone is an emerging concern globally. Failures of ceftriaxone treatment have been documented in Australia in strains that have reduced susceptibility to it (MICs above those of the wild type).

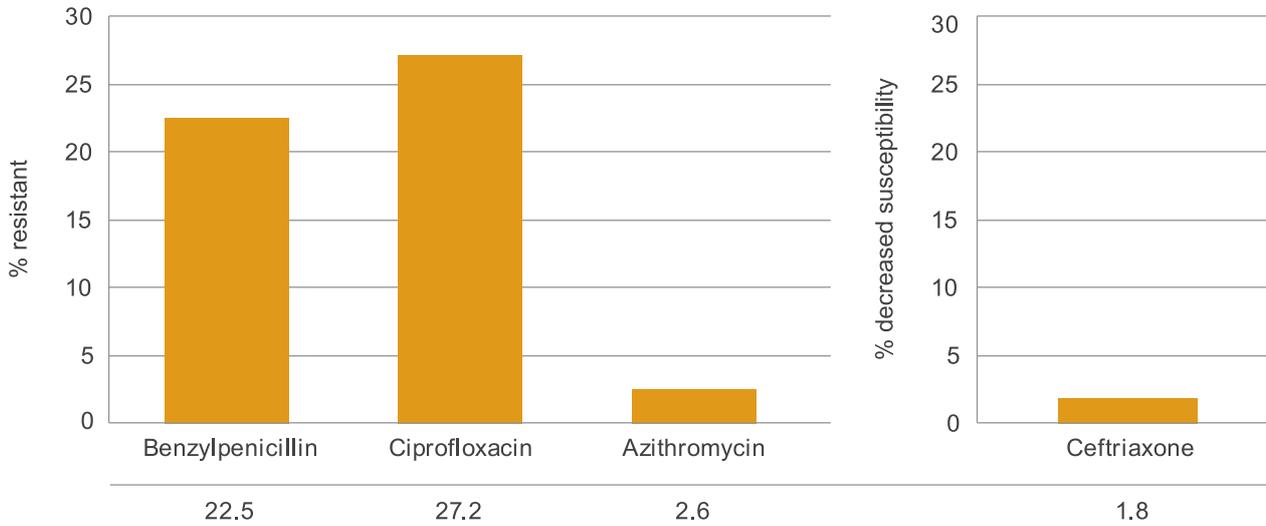
Key findings: national

In 2015, 22,720 cases of gonococcal infection were notified nationally (a rate of 95.5 per 100,000 population). Of these cases, 5,411 had positive laboratory cultures that were submitted for susceptibility testing. Most other cases would have been diagnosed without culture, using nucleic acid testing. Overall rates of resistance to the main agents used for treatment are shown in Figure 4.20. In these and subsequent data, all ceftriaxone percentages are presented as decreased susceptibility, rather than full resistance.

Key findings: states and territories

There was some variation in resistance rates to first-line agents across states and territories (Figure 4.21). Most noticeable are the low rates of resistance in the remote areas of the Northern Territory and Western Australia. A high proportion of the population in these parts of the country are Aboriginal and Torres Strait Islander people. Rates of decreased susceptibility to ceftriaxone exceed 5% in New South Wales and Victoria.

Figure 4.20: *Neisseria gonorrhoeae* resistance to individual antimicrobials used for treatment, 2015



Notes:

1. $n = 5,411$
2. Decreased susceptibility to ceftriaxone is defined as a minimum inhibitory concentration above that of the wild type; wild-type strains have no acquired resistance mechanisms.

Source: NNN (national)

National trends

In the past 16 years, resistance rates to the four main antimicrobials have evolved in different ways (Figure 4.22). Resistance to benzylpenicillin and ciprofloxacin trended upwards from 2003 to 2008, then declined somewhat, to stabilise at about 30%, which is not low enough to consider reintroducing them into standard treatment protocols. By 2015, there was early evidence of a downwards trend in resistance rates. Rates of reduced susceptibility to ceftriaxone and resistance to azithromycin are low; reduced susceptibility to ceftriaxone increased until 2013 but appears to be in decline, while resistance to azithromycin is slowly trending upwards (see Box 4.1).

Detailed reports of susceptibility data on *N. gonorrhoeae* from 1995 to 2014 can be found in the Australian Gonococcal Surveillance Programme annual reports.

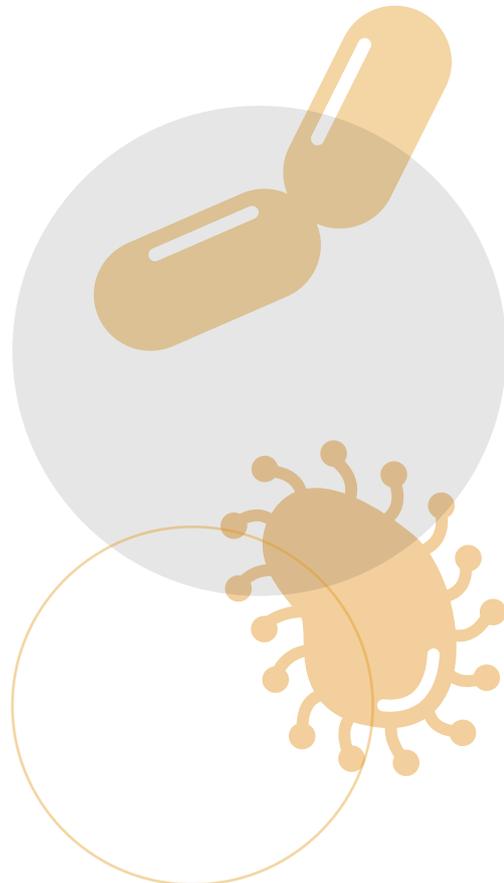
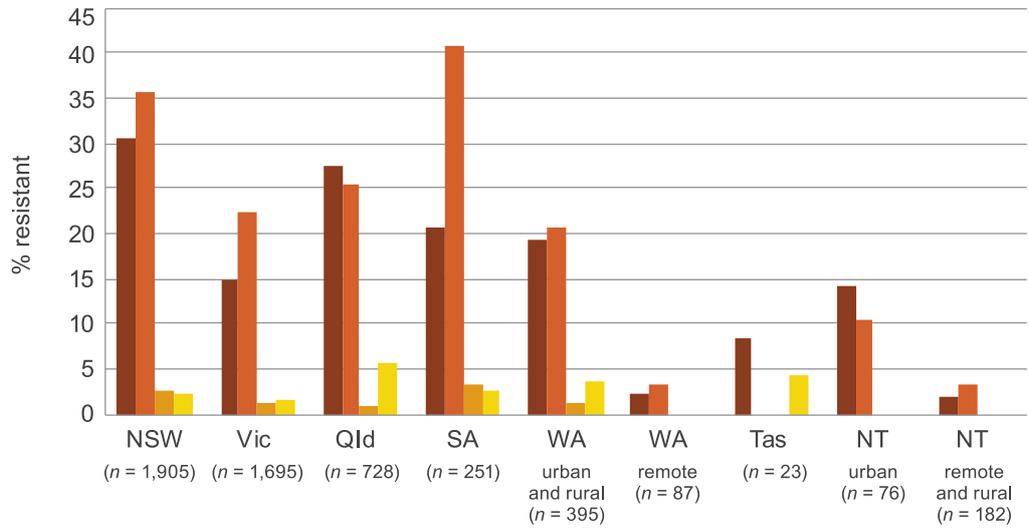


Figure 4.21: *Neisseria gonorrhoeae* resistance to individual antimicrobials used for treatment, by state and territory, 2015

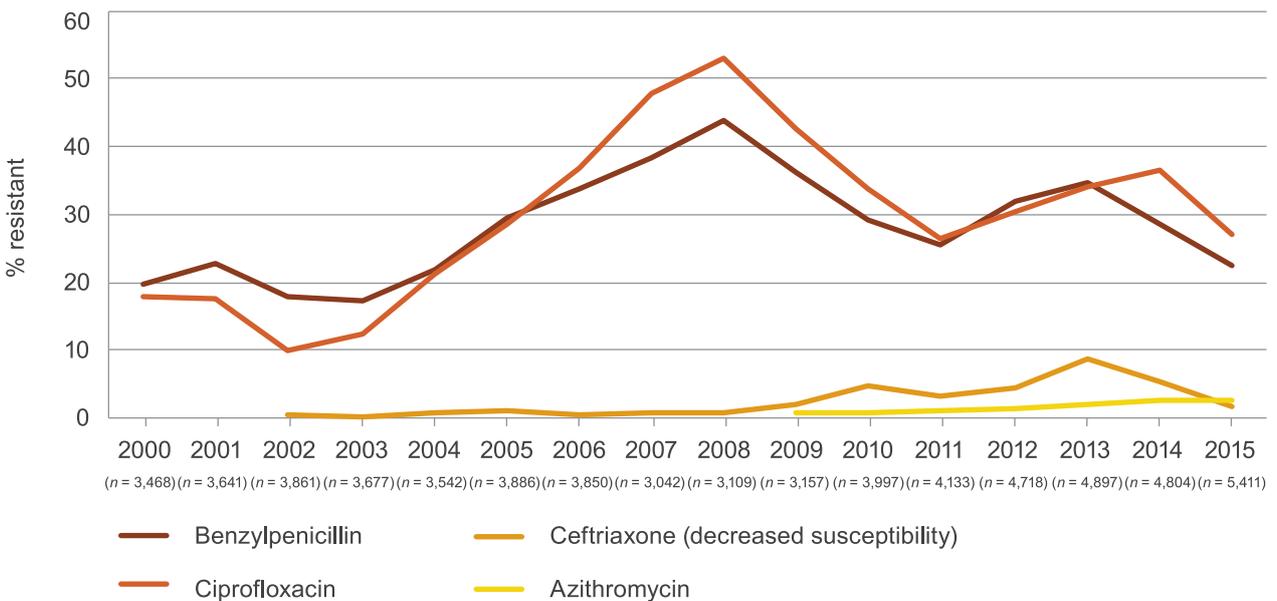


	NSW (n = 1,905)	Vic (n = 1,695)	Qld (n = 728)	SA (n = 251)	WA urban and rural (n = 395)	WA remote (n = 87)	Tas (n = 23)	NT urban (n = 76)	NT remote and rural (n = 182)
■ Benzylpenicillin	30.9	15.2	27.6	20.7	19.5	2.3	8.7	14.5	2.2
■ Ciprofloxacin	35.9	22.6	25.5	41.0	20.8	3.4	0.0	10.5	3.3
■ Ceftriaxone (decreased susceptibility)	2.7	1.5	1.0	3.6	1.3	0.0	0.0	0.0	0.0
■ Azithromycin	2.3	1.8	5.8	2.8	3.8	0.0	4.3	0.0	0.0

Note: Decreased susceptibility to ceftriaxone is defined as a minimum inhibitory concentration above that of the wild type; wild-type strains have no acquired resistance mechanisms.

Source: NNN (national)

Figure 4.22: Trends in resistance and multidrug-resistance patterns, and decreased susceptibility to ceftriaxone, in *Neisseria gonorrhoeae*, 2000–15



Note: Decreased susceptibility to ceftriaxone is defined as a minimum inhibitory concentration above that of the wild type; wild-type strains have no acquired resistance mechanisms.

Source: NNN (public and private hospitals, and health services)

● **Box 4.1: Monitoring azithromycin non-susceptibility in *Neisseria gonorrhoeae***

In 2015, 2.6% of *N. gonorrhoeae* clinical isolates were non-susceptible to azithromycin. This rate was higher than in 2013–14 (2.1–2.4%) and 2011–12 (1.1–1.3%). In 2015, Queensland had the highest proportion of resistant isolates (5.8% in 2015, up from 3.5% in 2014), followed by urban Western Australia (3.8%).

High-level resistance to azithromycin (minimum inhibitory concentration of ≥ 256 mg/L) was reported in Australia for the first time in 2013 and continues to be closely monitored by the National *Neisseria* Network for the Australian Gonococcal Surveillance Programme. In 2015, one isolate from New South Wales and one from urban Western Australia had high-level resistance to azithromycin.

Evidence of co-evolving cephalosporin and azithromycin non-susceptibility is being seen in other countries, and is of significant concern.

Molecular assays are increasingly being used in Australia to diagnose gonorrhoea. There are important advantages to using molecular diagnostic assays rather than culture for *N. gonorrhoeae* in terms of sensitivity, and robustness and reliability for remote settings where cultures may not survive transport. The primary disadvantage of molecular tests is that they currently cannot test for antimicrobial resistance. Where possible, culture and susceptibility testing should be requested and performed.

Annual reports of the Australian Gonococcal Surveillance Programme are published on the Australian Government Department of Health website (see Appendix 1).

4.7 *Neisseria meningitidis*

This section describes the health impact, treatment, types and impact of resistance, and key findings for resistance rates in *N. meningitidis*.

Health impact

N. meningitidis can cause septicaemia and meningitis, known as invasive meningococcal disease. Although this is a very uncommon infection in Australia as a result of the advent of vaccines that provide immunity to some strains, it is considered a medical emergency because it can progress rapidly to serious disease and death. Invasive meningococcal disease can be associated with outbreaks in environments that involve close prolonged contact between people, especially in the household. *N. meningitidis* is also rarely associated with localised disease, such as conjunctivitis, arthritis and pneumonia.

Treatment

Because invasive meningococcal disease is potentially life-threatening, most invasive infection is treated empirically (pending the results of blood cultures and, where necessary, testing of cerebrospinal fluid). The most important antimicrobials for treatment are ceftriaxone (or cefotaxime) and benzylpenicillin. Close contacts of patients with invasive meningococcal disease are given antimicrobial prophylaxis to prevent infection by clearing nasopharyngeal colonisation. The most important antimicrobials for prophylaxis are rifampicin, ciprofloxacin and ceftriaxone.

Types and impact of resistance

There is currently no international consensus on the definition of reduced susceptibility or resistance to benzylpenicillin in *N. meningitidis*.

In most test systems, wild-type strains (that is, strains with no acquired resistance mechanism) have MICs of 0.25 mg/L or less.

Resistance to benzylpenicillin and ceftriaxone has been slow to develop in Australia. Non-wild-type strains that have reduced susceptibility to these two agents are now found regularly, but are not yet associated with treatment failure. Occasional strains are found with resistance to rifampicin or reduced susceptibility to ciprofloxacin.

Resistance to benzylpenicillin and ceftriaxone has been slow to develop in Australia.

Key findings: national

In 2015, 254 cases of meningococcal infection were notified nationally (a rate of 1.1 per 100,000 population). From these cases, 117 isolates were submitted for susceptibility testing. Figure 4.23 shows the national rates

of resistance to the four key agents used for treatment or prophylaxis.

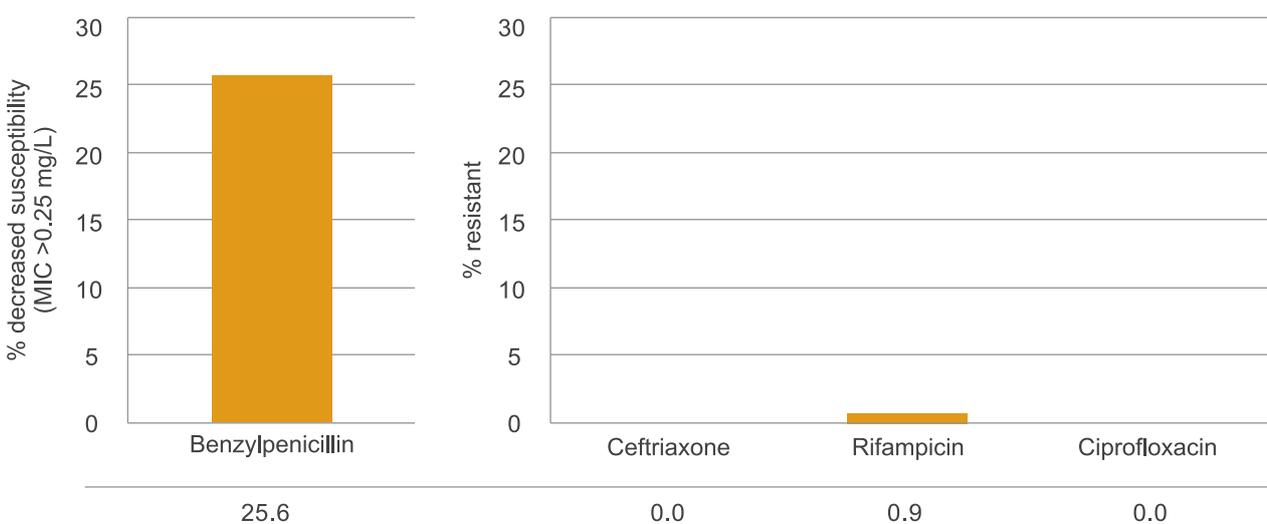
National trends

In the past 16 years, there has been little change in the (very low or zero) rates of resistance to any of the four key agents, except for benzylpenicillin (Figure 4.24). For benzylpenicillin, in this report, resistance is defined as an MIC of ≥ 1 mg/L. In contrast, the rates of reduced susceptibility to benzylpenicillin (defined in this report as an MIC of >0.25 mg/L) have shown a slow but steady increase (Figure 4.25).

Rates of reduced susceptibility to benzylpenicillin have shown a slow but steady increase.

Detailed reports of susceptibility data on *N. meningitidis* from 1997 to 2015 can be found in the Australian Meningococcal Surveillance Programme annual reports.

Figure 4.23: *Neisseria meningitidis* resistance to individual antimicrobials used for treatment and prophylaxis, 2015

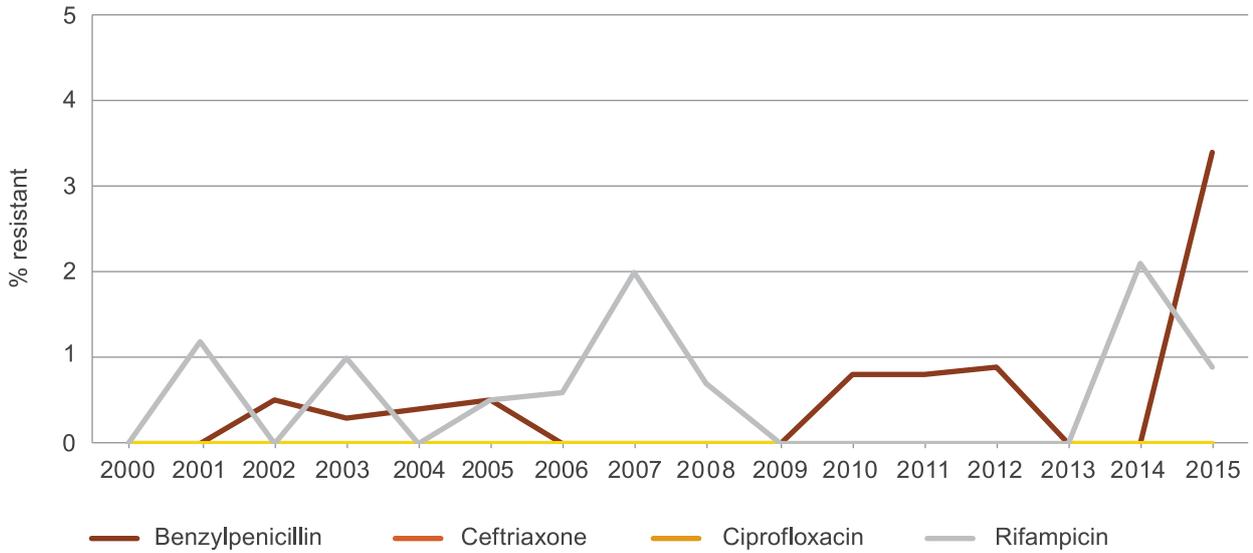


Notes:

1. $n = 117$
2. Decreased susceptibility or resistance to benzylpenicillin: in most test systems, wild-type strains (i.e. with no acquired resistance mechanism) have minimum inhibitory concentrations of ≤ 0.25 mg/L.

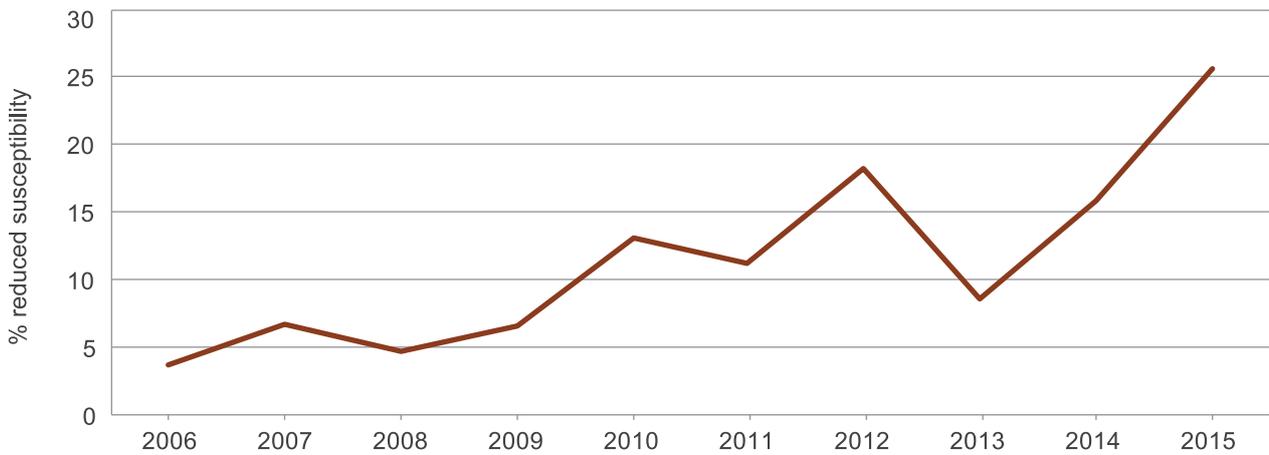
Source: NNN (public and private hospitals, and health services)

Figure 4.24: Sixteen-year trends in resistance in *Neisseria meningitidis*



Note: Resistance to benzylpenicillin is defined as a minimum inhibitory concentration of ≥ 1 mg/L.
 Source: NNN (public and private hospitals, and health services)

Figure 4.25: Ten-year trends in reduced susceptibility to benzylpenicillin in *Neisseria meningitidis*



Note: Reduced susceptibility is defined as a minimum inhibitory concentration of >0.25 mg/L.
 Source: NNN (public and private hospitals, and health services)

4.8 *Pseudomonas aeruginosa*

This section describes the health impact, treatment, types and impact of resistance, and key findings for resistance rates in *P. aeruginosa*.

Health impact

P. aeruginosa is an opportunistic, nosocomial pathogen that primarily affects hospitalised or immunocompromised patients. It is a ubiquitous organism found in moist environments. It is naturally resistant to many chemicals, including most common antimicrobials and some antiseptics. As a consequence, it frequently causes infections in patients who are receiving antimicrobial treatments for other purposes.

P. aeruginosa can cause urinary tract infection in catheterised patients and patients with structural abnormalities of the urinary tract. It is associated with burn and other wound infections, and has a strong propensity to cause chronic, persistent airway infection in patients with cystic fibrosis. It also causes septicaemia, especially in neutropenic patients.

Treatment

P. aeruginosa is susceptible to only a limited range of antimicrobials:

- Specialised β -lactams such as piperacillin (with or without tazobactam), ceftazidime and meropenem
- Aminoglycosides such as gentamicin and tobramycin
- Some fluoroquinolones, such as ciprofloxacin.

Urinary tract infections can often be managed with oral fluoroquinolones; more serious infections must be treated with β -lactams, which may be used in combination with aminoglycosides for the most serious infections. The effective β -lactams and the aminoglycosides can only be administered intravenously.

Types and impact of resistance

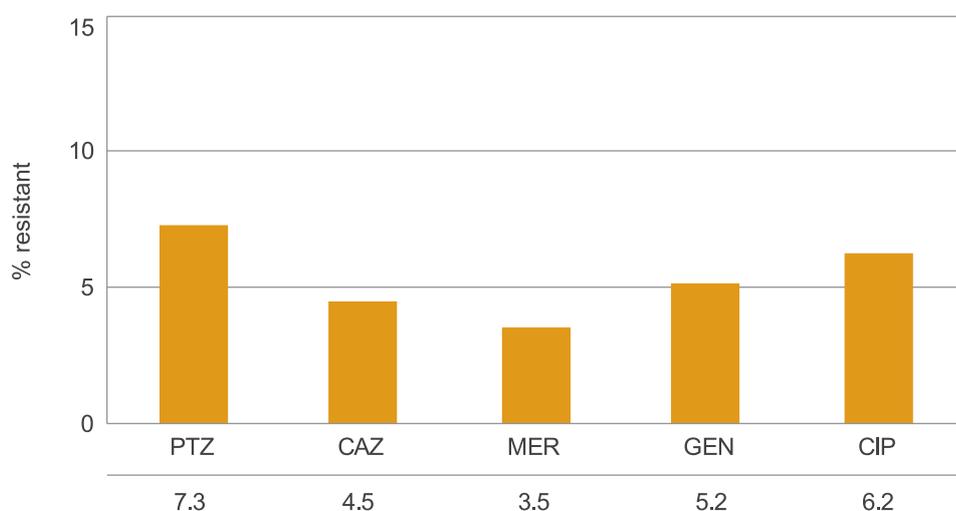
This species is intrinsically resistant to many antimicrobial classes as a result of the presence of several efflux pumps in its cell wall and cell membrane. It is notorious for its capacity to become resistant during treatment to the limited range of effective agents, mainly as a result of upregulation of these efflux pumps. It also has the capacity to become resistant to β -lactams through porin loss and the acquisition of β -lactamases. Multidrug-resistant strains with acquired resistance to two or three of the effective antimicrobial classes will require other treatments, such as the potentially toxic colistin.

Pseudomonas aeruginosa is intrinsically resistant to many antimicrobial classes.

Key findings: national

Resistance of *P. aeruginosa* to key antimicrobial agents is shown in Figure 4.26. Rates of resistance were substantially higher in public hospitals (Figure 4.27), possibly due in part to the influence of isolates from patients with cystic fibrosis who are managed in the public sector. These patients have isolates with higher rates of resistance to all effective agents because they are likely to have been treated multiple times for acute infective exacerbations of cystic fibrosis lung disease.

Figure 4.26: *Pseudomonas aeruginosa* resistance to individual agents, 2015

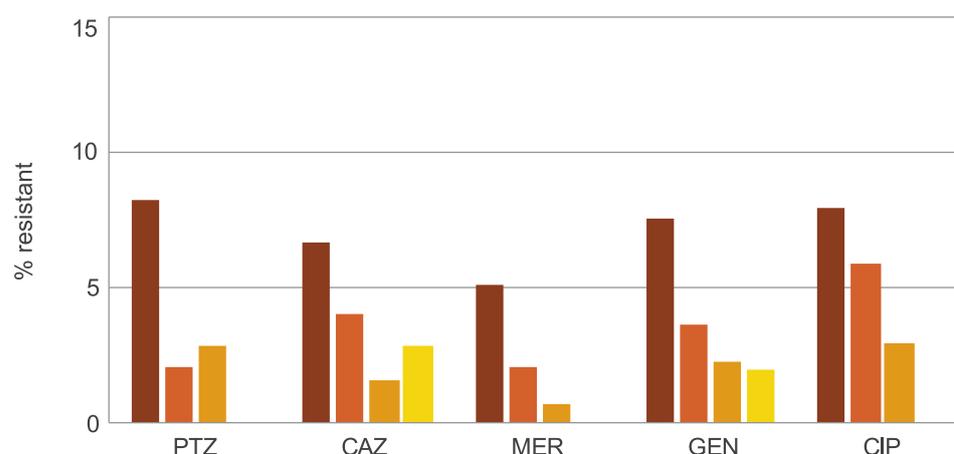


CAZ = ceftazidime; CIP = ciprofloxacin; GEN = gentamicin; MER = meropenem; PTZ = piperacillin-tazobactam

Note: *n* = 35,270

Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

Figure 4.27: *Pseudomonas aeruginosa* resistance, by clinical setting, 2015



Public hospitals (<i>n</i> = 18,668)	8.1	6.6	5.1	7.4	7.8
Private hospitals (<i>n</i> = 5,423)	2.0	3.9	2.0	3.5	5.8
Community (<i>n</i> = 9,853)	2.8	1.5	0.6	2.2	2.9
Aged care home (<i>n</i> = 1,326)	0.0	2.8	-	2.0	-

- = not available (either not tested or tested against an inadequate number of isolates); CAZ = ceftazidime; CIP = ciprofloxacin; GEN = gentamicin; MER = meropenem; PTZ = piperacillin-tazobactam

Sources: AGAR and National Passive AMR Surveillance System (OrgTRx) (public hospitals); AGAR, OrgTRx (SA) and SNP (private hospitals); OrgTRx (SA) and SNP (community)

4.9 *Salmonella* species

This section describes the health impact, treatment, types and impact of resistance, and key findings for resistance rates in *Salmonella* species.

Health impact

Salmonella species are important causes of bacterial gastroenteritis. Most cases are acquired through foodborne transmission. Occasionally, gastroenteritis is complicated by septicaemia, although this is usually self-limiting. Two serotypes, *Salmonella* Typhi and *Salmonella* Paratyphi (together called ‘typhoidal *Salmonella*’), cause a distinct syndrome called enteric fever, in which the organism is always invasive (causing septicaemia), and causes significant morbidity and mortality if untreated. *Salmonella* gastroenteritis is endemic in Australia, but almost all cases of enteric fever are seen in returning overseas travellers.

Treatment

Salmonella gastroenteritis is self-limiting. Antimicrobial therapy is generally contraindicated because it does not affect the course of the disease and will prolong intestinal carriage of the organism after disease resolution, increasing the risk of transmission. Antimicrobial therapy is indicated in patients with severe disease or septicaemia (typhoidal *Salmonella* infection, in particular), and patients who have prosthetic vascular grafts. Ciprofloxacin, azithromycin and ceftriaxone are the standard treatments.

Types and impact of resistance

Resistance to older treatment agents, such as ampicillin and chloramphenicol, has been seen for many years. So far, resistance to the newer agents has only been a problem with ciprofloxacin and other fluoroquinolones, such as norfloxacin. This has resulted in recent

reassessment of the definition of fluoroquinolone resistance. Not all susceptibility testing systems are yet capable of applying the new definitions.

Key findings: national

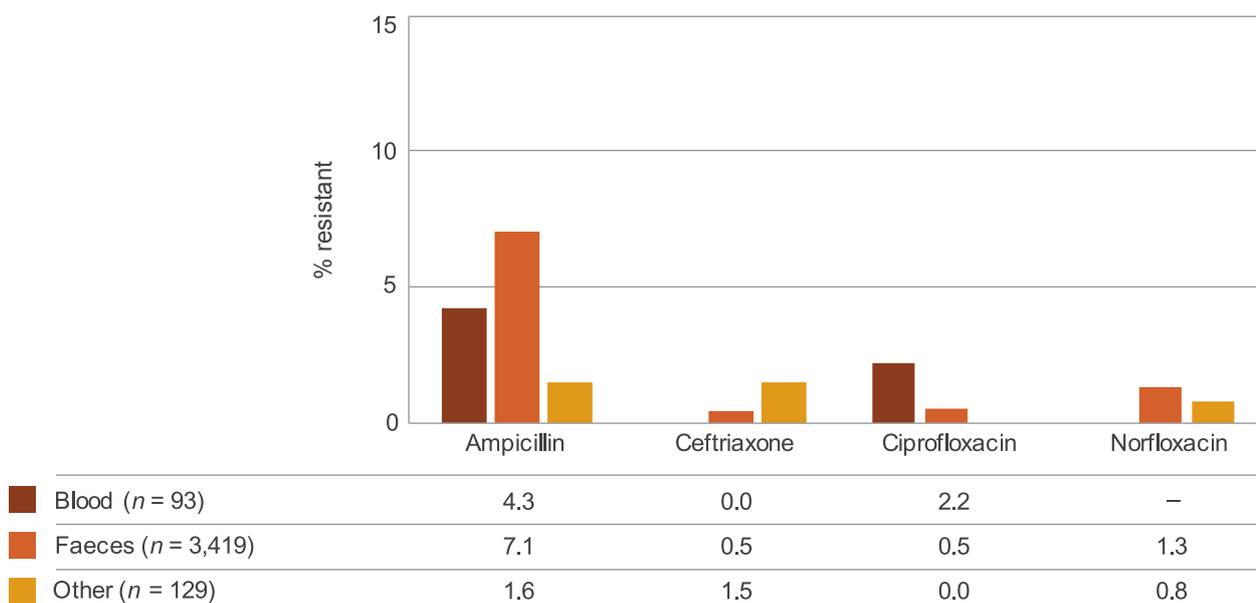
In non-typhoidal *Salmonella* species, rates of resistance were low for ampicillin, and very low for ceftriaxone and the fluoroquinolones (Figure 4.28). In contrast, rates of resistance in typhoidal *Salmonella* species to the fluoroquinolone ciprofloxacin were above 50% for blood isolates (Figure 4.29).

In non-typhoidal Salmonella species, rates of resistance were low for ampicillin, and very low for ceftriaxone and the fluoroquinolones. In contrast, rates of resistance in typhoidal Salmonella species to the fluoroquinolone ciprofloxacin were above 50% for blood isolates.

Additional findings from targeted surveillance on blood culture isolates

Additional data on 30-day all-cause mortality for strains causing septicaemia and enteric fever are available from AGAR. There was no mortality at 30 days for typhoidal strains, and five deaths related to non-typhoidal strains (Table 4.13).

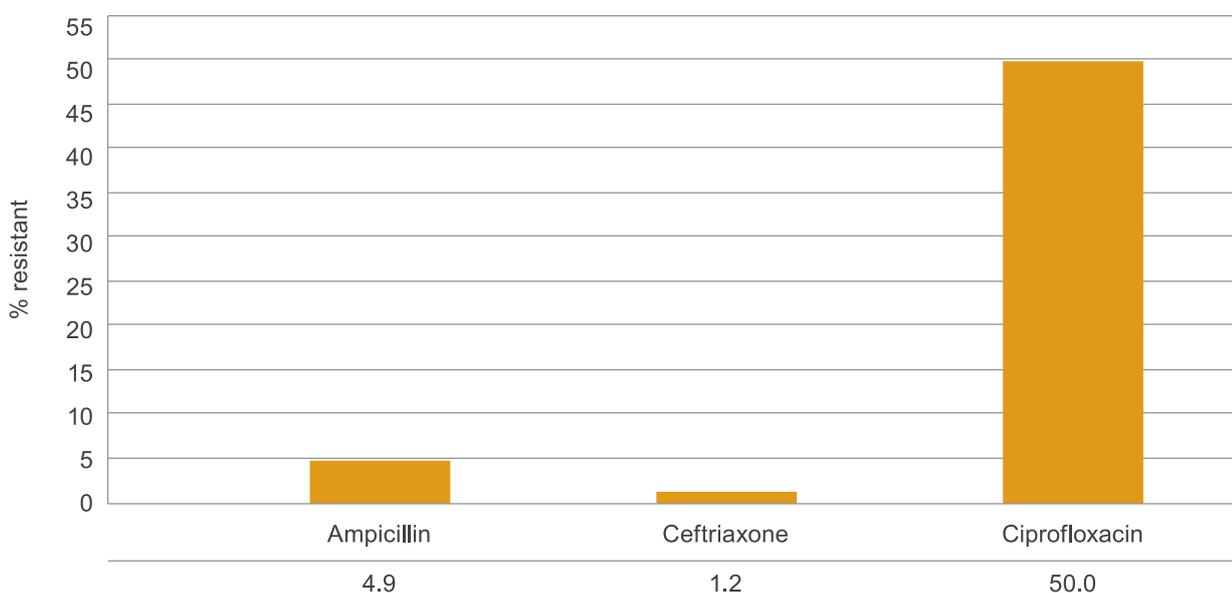
Figure 4.28: Non-typhoidal *Salmonella* species resistance, by specimen source, 2015



- = not available (either not tested or tested against an inadequate number of isolates)

Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

Figure 4.29: Typhoidal *Salmonella* species resistance (blood culture isolates), 2015



Note: n = 82

Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

Table 4.13: Onset setting and 30-day all-cause mortality for infections with *Salmonella* species (blood culture isolates), 2015

Species	Community, <i>n</i>	Community mortality, % (<i>n</i>)	Hospital, <i>n</i>	Hospital mortality, % (<i>n</i>)	Total, <i>n</i>	Total mortality, % (<i>n</i>)
<i>Salmonella</i> species (non-typhoidal)	61	3.3 (2)	12	25.0 (3)	73	6.8 (5)
<i>Salmonella</i> species (typhoidal)	13	0.0 (0)	0	0.0 (0)	13	0.0 (0)
Total	74	2.7 (2)	12	25.0 (3)	86	5.8 (5)

Source: AGAR (national)

4.10 *Shigella* species

This section describes the health impact, treatment, types and impact of resistance, and key findings for resistance rates in *Shigella* species.

Health impact

Shigella species are an uncommon but important cause of gastroenteritis. Genetically, they are almost identical to *E. coli*, and have a similar capacity to acquire multiple antimicrobial resistances. They also have the capacity to cause outbreaks if there is a common source(s) that infects people, or through person-to-person transmission.

Treatment

Treatment is usually administered when the infection is confirmed to be due to *Shigella*. The main aim of treatment is to prevent transmission of the organism, rather than to treat symptoms. The antimicrobials of choice are fluoroquinolones (ciprofloxacin and norfloxacin) and trimethoprim-sulfamethoxazole.

Types and impact of resistance

Resistance, including multi-drug resistance to conventional treatments, is well documented in other countries. Azithromycin is considered a suitable option for infections caused by strains that are resistant to standard treatments.

Definitions of resistance to azithromycin are under development and not yet available.

Key findings: national

Resistance to ampicillin was common in *S. flexneri*. The prevalence of resistance to ciprofloxacin and ceftriaxone was very low in *S. flexneri*, but substantial in *S. sonnei* (Figure 4.30). The presence of any resistance to ciprofloxacin in Australia is of concern, given the capacity of this organism to cause outbreaks.

The presence of any resistance to ciprofloxacin in Shigella species is of concern, given the capacity of this organism to cause outbreaks.

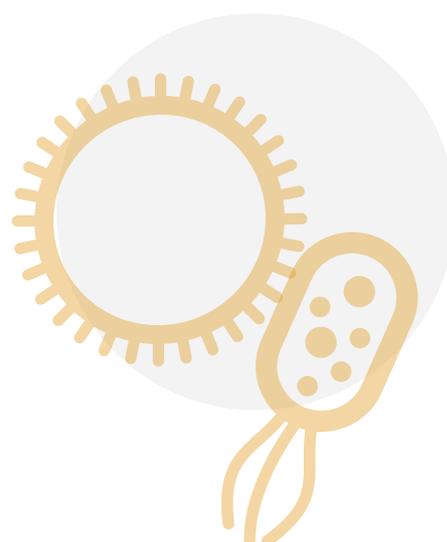
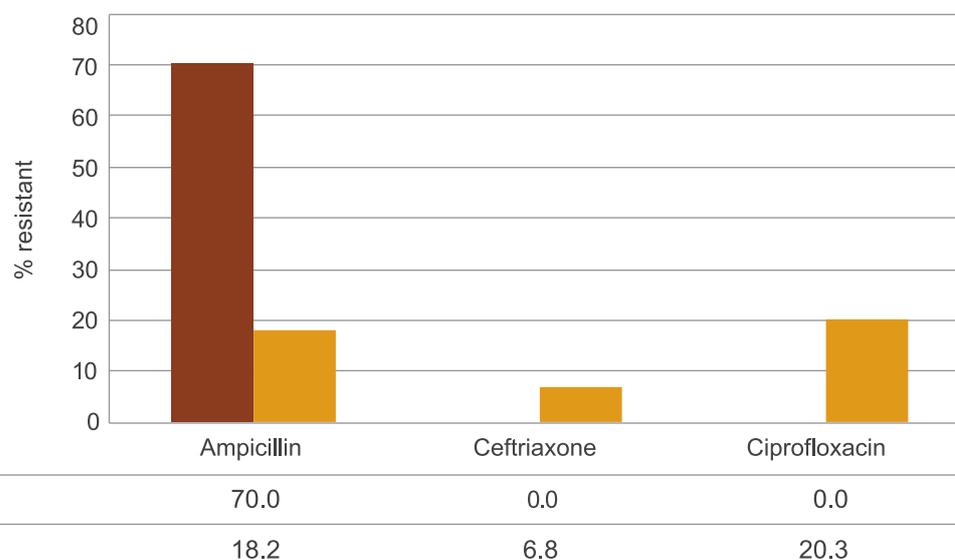


Figure 4.30: *Shigella* species resistance (faecal isolates), 2015



Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

4.11 *Staphylococcus aureus*

This section describes the health impact, treatment, types and impact of resistance, and key findings for resistance rates in *S. aureus*.

Health impact

S. aureus is a common human pathogen that causes a wide range of infections, including minor infections such as boils, impetigo and wound infections; moderate infections such as cellulitis; and serious infections such as bone and joint infections, pneumonia, endocarditis and septicaemia. Infections associated with bacteraemia (positive blood cultures) have a 30-day crude mortality of 15–30%. *S. aureus* is also a common cause of healthcare-associated infections, especially surgical site infections, intravascular line infections with bacteraemia, and infections of prosthetic devices.

According to AGAR data, the overall 30-day all-cause mortality rate for *S. aureus* bacteraemia in 2015 was 16.0%; it was higher in hospital-onset bacteraemia than in the community. Thirty-day all-cause mortality was lowest with methicillin-susceptible strains, higher for community-associated bacteraemia, and highest

for hospital-associated bacteraemia. Common clinical manifestations of staphylococcal bacteraemia were skin and skin structure infections, bone and joint infections, and device-related infections (Table 4.14). With the exception of right-sided endocarditis, all infections are more common in males.

Treatment

Many staphylococcal skin infections can often be managed without antimicrobial therapy, but moderate and serious infections require treatment. The preferred agent for ‘susceptible’ strains is flucloxacillin (or dicloxacillin), which can be replaced with first-generation cephalosporins such as cefazolin or cefalexin in penicillin-allergic patients.

Table 4.14: Principal clinical manifestations of *Staphylococcus aureus* infection (blood culture isolates), 2015

Principal clinical manifestation	Male	Female	Total
Skin and skin structure infection	272	146	418
Osteomyelitis/septic arthritis	283	121	404
Device-related infection without metastatic focus	232	122	354
No focus (setting known; e.g. in febrile neutropenia)*	23	11	34
Febrile neutropenia (when specified)*	17	14	31
No focus (setting not known)*	172	101	273
Other clinical syndrome	82	44	126
Pneumonia/empyema	83	40	123
Endocarditis, left-sided	75	46	121
Deep abscess(es), excluding those in the central nervous system	59	30	89
Endocarditis, right-sided	26	28	54
Central nervous system infection - meningitis, abscess(es)	32	14	46
Device-related infection with metastatic focus	18	13	31
Urinary tract infection	4	0	4
Intra-abdominal infection other than biliary tract	1	0	1
Endocarditis, native valve, unspecified	1	0	1
Total	1,380	730	2,110

* These principal clinical manifestations reflect the variation in reporting by contributors.
Source: AGAR (national)

Types and impact of resistance

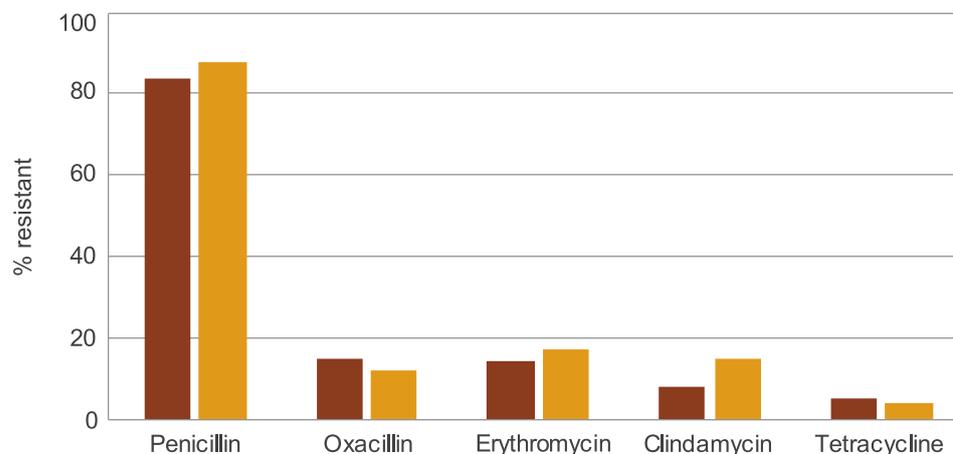
Around 85–90% of strains in the community are resistant to penicillin; this has been the case for decades. Healthcare-associated strains that are resistant to flucloxacillin and first-generation cephalosporins, commonly called methicillin-resistant *S. aureus* (MRSA), emerged in the 1970s and are now common in many parts of Australia. These healthcare-associated clones are multidrug resistant and require treatment with reserve antimicrobials such as vancomycin, rifampicin and fusidic acid. Community-associated clones of MRSA are distinct from healthcare-associated clones and emerged in the 1980s. These clones are usually not multidrug resistant, and moderate infections may be treated with trimethoprim-sulfamethoxazole or clindamycin. All serious

MRSA infections require initial treatment with vancomycin. Resistance to vancomycin appears to be uncommon, but is difficult to detect in the diagnostic laboratory. There are very few alternative treatments to vancomycin.

Key findings: national

Overall, more than 80% of *S. aureus* isolates were resistant to benzylpenicillin in 2015 (Figure 4.31). Oxacillin (methicillin) resistance was 15% in isolates from blood and 12% in other specimens. There was little difference in rates of resistance between different clinical settings, apart from oxacillin resistance, which was higher in public hospitals and health services, and aged care homes, lower in private hospitals, and lowest in the community (Figure 4.32).

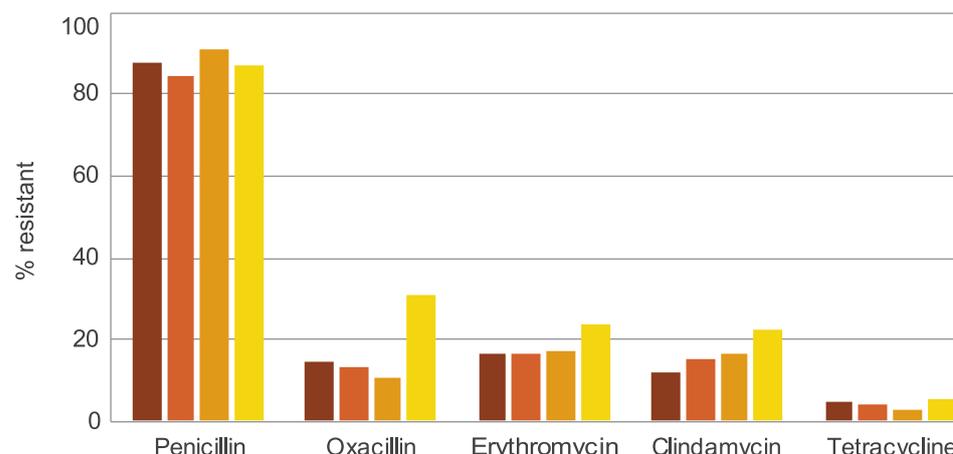
Figure 4.31: *Staphylococcus aureus* resistance, by specimen source, 2015



■ Blood (<i>n</i> = 5,179)	83.2	15.0	14.4	8.1	5.2
■ Other (<i>n</i> = 104,914)	87.6	11.8	17.0	14.6	4.1

Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

Figure 4.32: *Staphylococcus aureus* resistance, by clinical setting, 2015



■ Public hospitals (<i>n</i> = 55,451)	87.9	14.5	16.3	12.1	4.9
■ Private hospitals (<i>n</i> = 14,357)	84.5	13.1	16.2	15.6	3.9
■ Community (<i>n</i> = 38,142)	91.1	10.7	17.5	16.5	3.1
■ Aged care home (<i>n</i> = 2,175)	87.2	30.8	23.8	22.1	5.7

Sources: AGAR and National Passive AMR Surveillance System (OrgTRx) (public hospitals); AGAR, OrgTRx (SA) and SNP (private hospitals); OrgTRx (SA) and SNP (community and aged care homes)

*Oxacillin (methicillin) resistance in *S. aureus* was 15% in isolates from blood.*

Resistance of MRSA to ciprofloxacin and erythromycin is high, especially in blood isolates. A small number of MRSA strains exhibited resistance to linezolid and daptomycin (Figure 4.33). There were noticeable differences in resistance to ciprofloxacin, erythromycin and gentamicin in MRSA strains between clinical settings (Figure 4.34), possibly related to variation in the distribution of healthcare-associated clones compared with community-associated clones (Figures 4.35 and 4.36).

Healthcare-associated clones of MRSA had high rates of resistance to ciprofloxacin and erythromycin, and moderate rates of resistance to clindamycin, trimethoprim-sulfamethoxazole and gentamicin (Figure 4.35). Rates of resistance to other 'anti-MRSA' agents are low. Rates of resistance to ciprofloxacin and erythromycin

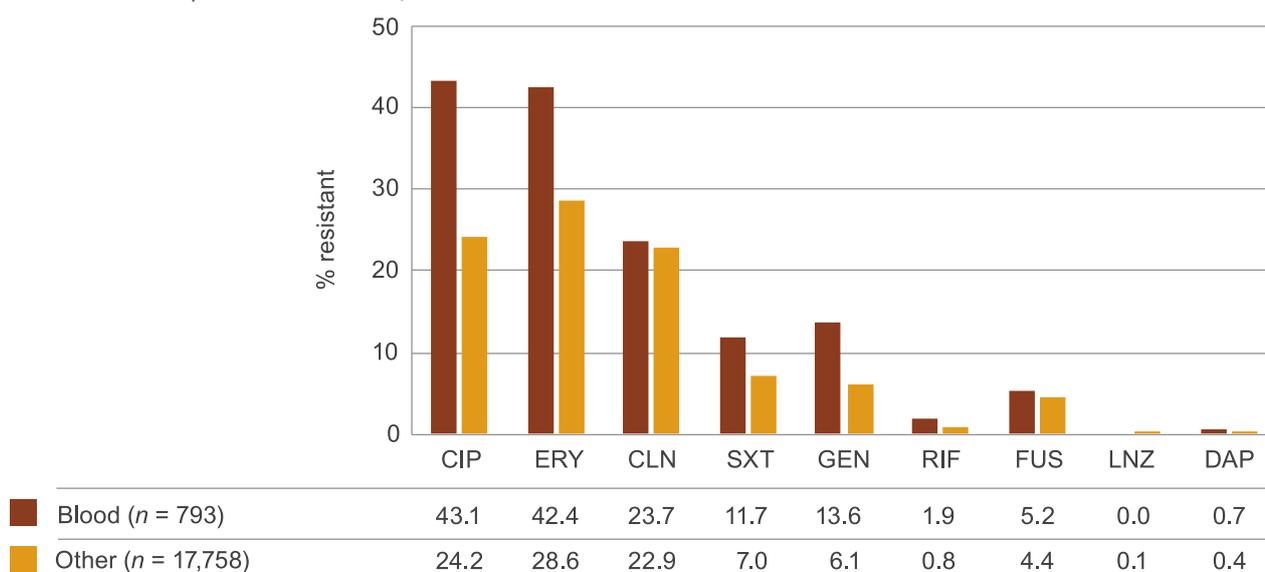
were much lower in community-associated clones than in healthcare-associated clones (Figure 4.36).

Table 4.15 shows the multilocus sequence types of MRSA clones across Australia. Community-associated clones dominate in staphylococcal bacteraemia.

Key findings: states and territories

State and territory data on blood culture isolates are available from the AGAR targeted surveillance program. There are substantial differences among the states and territories in the prevalence and types of MRSA. Overall rates range from 5.9% in Tasmania to 37.3% in the Northern Territory (Figure 4.37 and *AURA 2016: supplementary data*). Community-associated MRSA clones dominate in all states and territories except the Australian Capital Territory, New South Wales and Tasmania. Multilocus sequence type analysis reveals a great diversity of clones across the states and territories (Figure 4.38).

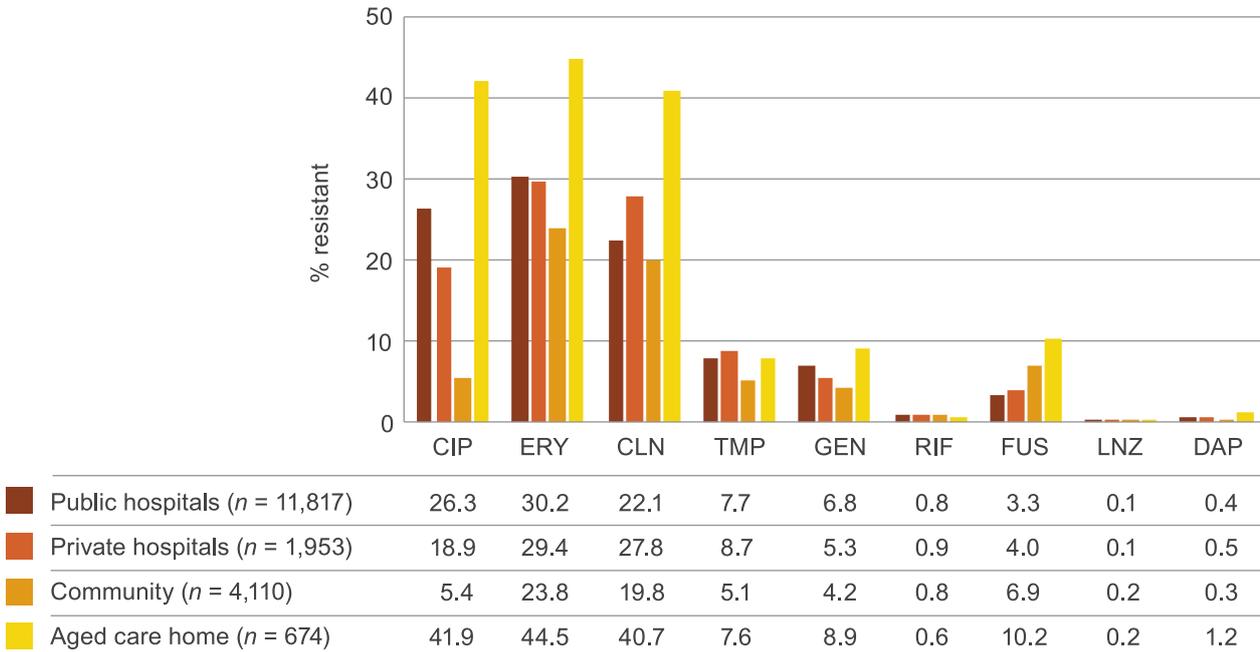
Figure 4.33: Methicillin-resistant *Staphylococcus aureus* resistance to non- β -lactam agents, by specimen source, 2015



CIP = ciprofloxacin; CLN = clindamycin; DAP = daptomycin; ERY = erythromycin; FUS = fusidic acid; GEN = gentamicin; LNZ = linezolid; RIF = rifampicin; SXT = trimethoprim-sulfamethoxazole

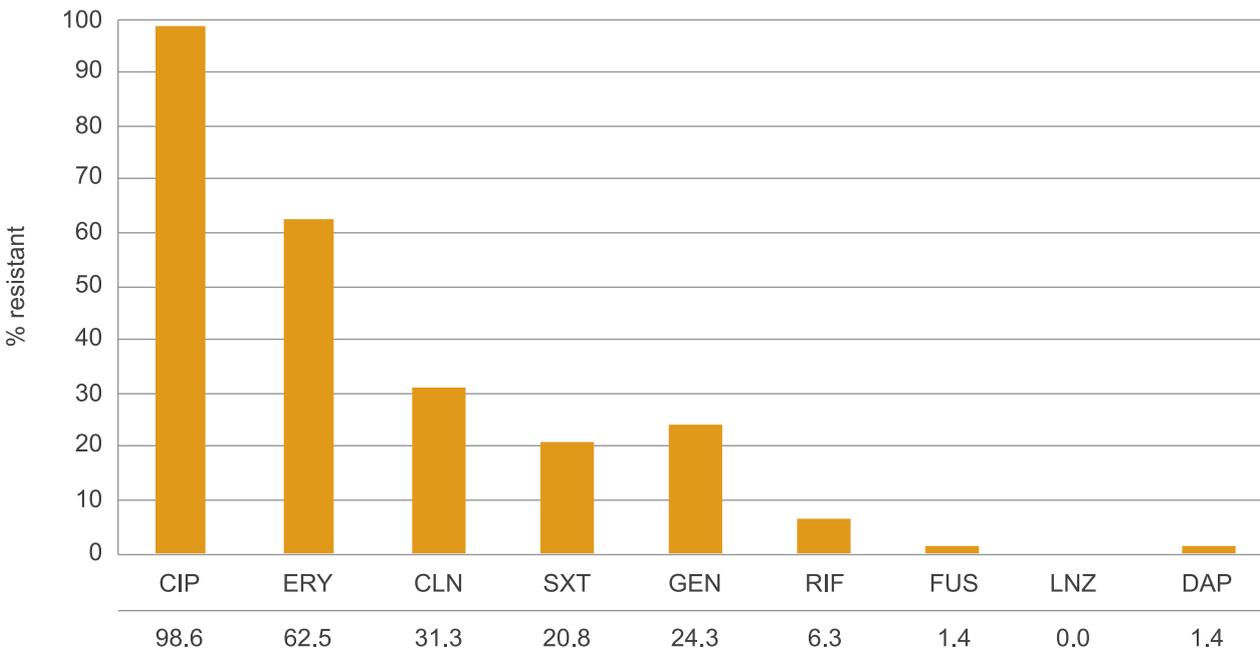
Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

Figure 4.34: Methicillin-resistant *Staphylococcus aureus* resistance to non-β-lactam agents, by clinical setting, 2015



CIP = ciprofloxacin; CLN = clindamycin; DAP = daptomycin; ERY = erythromycin; FUS = fusidic acid; GEN = gentamicin; LNZ = linezolid; RIF = rifampicin; SXT = trimethoprim-sulfamethoxazole
 Sources: AGAR (public hospitals); National Passive AMR Surveillance System (OrgTRx) (public hospitals and health services); AGAR and SNP (private hospitals); SNP (community and aged care homes)

Figure 4.35: Resistance to other antimicrobials of healthcare-associated clones of methicillin-resistant *Staphylococcus aureus* (blood culture isolates), 2015



CIP = ciprofloxacin; CLN = clindamycin; DAP = daptomycin; ERY = erythromycin; FUS = fusidic acid; GEN = gentamicin; LNZ = linezolid; RIF = rifampicin; SXT = trimethoprim-sulfamethoxazole
 Note: n = 144
 Source: AGAR (national)

Table 4.15: Methicillin-resistant *Staphylococcus aureus* clones (blood culture isolates), 2015

MRSA type	Clone	Clonal complex	<i>n</i>	%	
Healthcare associated	ST22-IV (EMRSA-15)*		22	108	25.4
	ST239-III (Aus2/3 EMRSA)†		8	34	8.0
	ST36-II (EMRSA-16/USA200)		30	1	0.2
	ST225-II (NY/Japan/USA100 variant)		5	1	0.2
	Total			144	33.8
Community associated	ST93-IV (Qld CA-MRSA)	Singleton		89	20.9
	ST45-V (WA84 MRSA)		45	41	9.6
	ST5-IV		5	34	8.0
	ST1-IV (WA1 MRSA)		1	30	7.0
	ST30-IV (SWP MRSA)		30	17	4.0
	ST78-IV (WA2 MRSA)		78	12	2.8
	ST5-V		5	7	1.6
	ST872-IV		1	5	1.2
	ST8-IV		8	5	1.2
	ST1-I		1	4	0.9
	ST762-IV		1	3	0.7
	Other clones (<i>n</i> = 25)			35	8.2
	Total			282	66.1

MRSA = methicillin-resistant *Staphylococcus aureus*

* Includes two isolates identified as ST22slv-IV

† Includes four isolates identified as ST239slv

Source: AGAR (national)

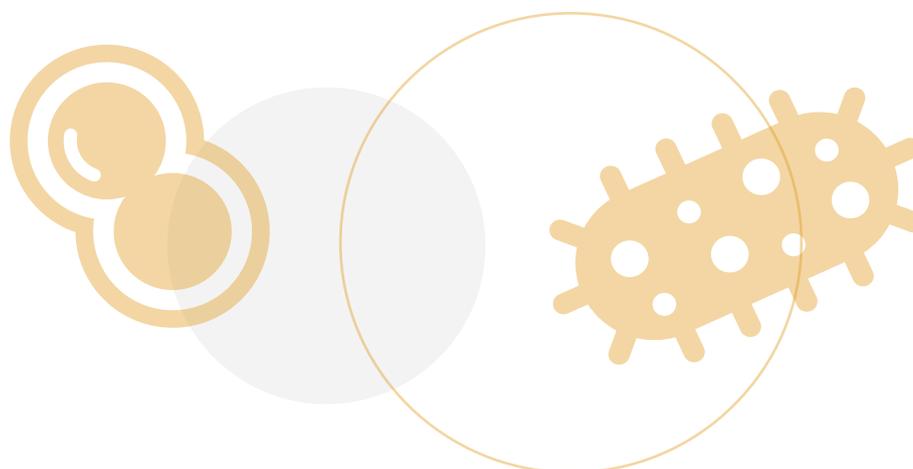
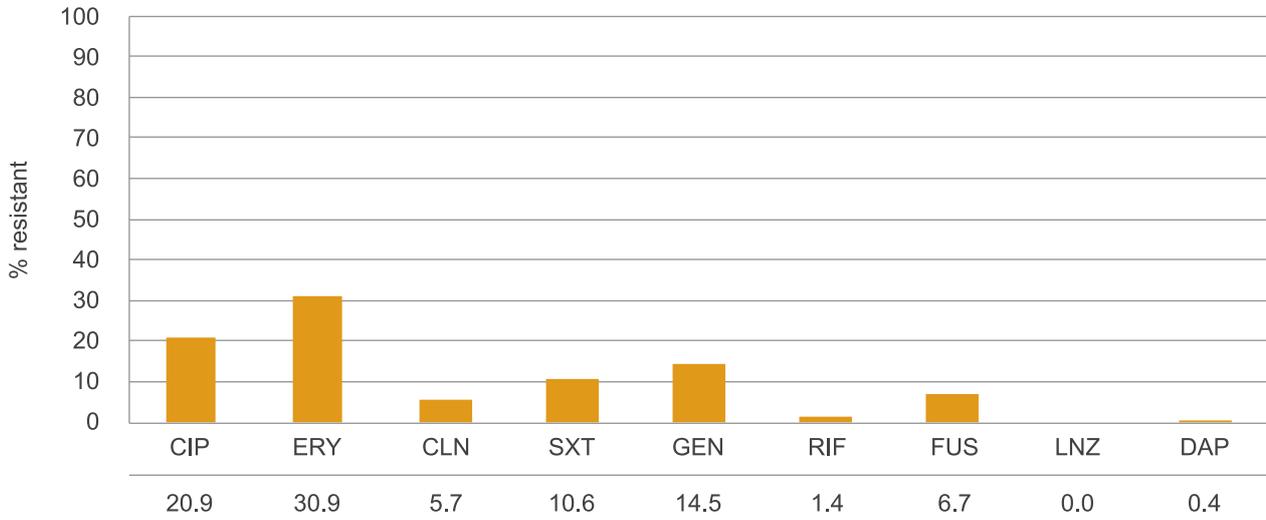
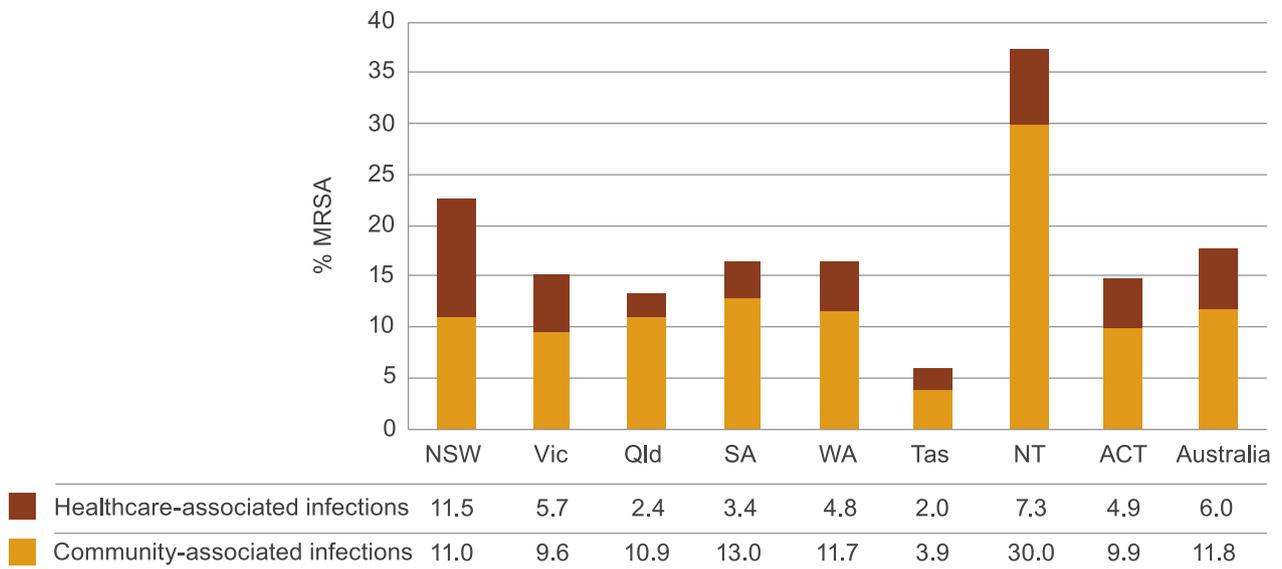


Figure 4.36: Resistance to other antimicrobials of community-associated clones of methicillin-resistant *Staphylococcus aureus* (blood culture isolates), 2015



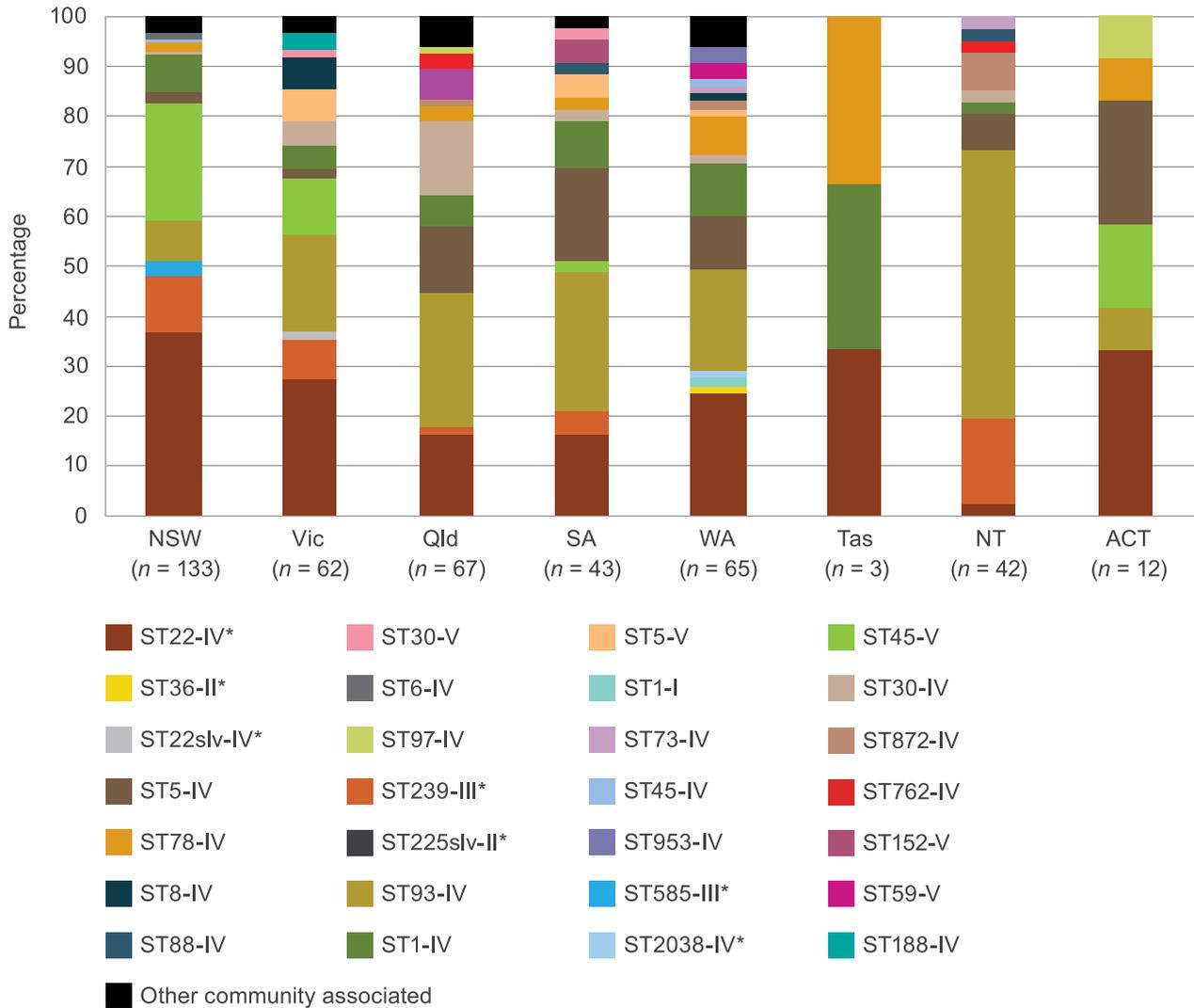
CIP = ciprofloxacin; CLN = clindamycin; DAP = daptomycin; ERY = erythromycin; FUS = fusidic acid; GEN = gentamicin; LNZ = linezolid; RIF = rifampicin; SXT = trimethoprim-sulfamethoxazole
 Note: n = 282
 Source: AGAR (national)

Figure 4.37: Methicillin-resistant *Staphylococcus aureus* as a percentage of all *S. aureus* isolates, by state and territory (blood culture isolates), 2015



MRSA = methicillin-resistant *Staphylococcus aureus*
 Source: AGAR (national)

Figure 4.38: Distribution of methicillin-resistant *Staphylococcus aureus* clones, by state and territory (blood culture isolates), 2015



MRSA = methicillin-resistant *Staphylococcus aureus*
 * Healthcare-associated clones
 Source: AGAR (national)

There are substantial differences among the states and territories in the prevalence and types of MRSA. Overall rates range from 5.9% in Tasmania to 37.3% in the Northern Territory.

The overall 30-day all-cause mortality rate was 16.0%; it was higher in hospital-onset bacteraemia than in community-onset bacteraemia (Table 4.16). Thirty-day all-cause mortality was lowest with methicillin-susceptible strains, somewhat higher for bacteraemia caused by community-associated MRSA clones, and highest for bacteraemia caused by hospital-associated MRSA clones.

Full data from AGAR surveys of *S. aureus* can be found on the AGAR website.

Table 4.16: Onset setting and 30-day all-cause mortality for infections with *Staphylococcus aureus* (blood culture isolates), 2015

<i>Staphylococcus aureus</i> strain	Community, <i>n</i>	Community mortality, % (<i>n</i>)	Hospital, <i>n</i>	Hospital mortality, % (<i>n</i>)	Total, <i>n</i>	Total mortality, % (<i>n</i>)
Methicillin susceptible	1,264	15.3 (194)	366	15.0 (55)	1,630	15.3 (249)
Methicillin resistant	247	19.4 (48)	109	18.3 (20)	356	19.1 (68)
Community-associated MRSA clones	162	17.3 (28)	56	17.9 (10)	218	17.4 (38)
Hospital-associated MRSA clones	81	24.7 (20)	49	20.4 (10)	130	23.1 (30)
Not determined	4	0.0 (0)	4	0.0 (0)	8	0.0 (0)
Total	1,511	16.0 (242)	475	15.8 (75)	1,986	16.0 (317)

MRSA = methicillin-resistant *Staphylococcus aureus*
 Source: AGAR (national)

4.12 *Streptococcus agalactiae*

This section describes the health impact, treatment, types and impact of resistance, and key findings for resistance rates in *S. agalactiae*.

Health impact

S. agalactiae, also called group B *Streptococcus* (GBS), occasionally causes infections similar to those caused by *S. pyogenes*. These include skin and soft tissue infections, as well as more serious infections, such as septicaemia, and bone and joint infections. Its greatest significance is as the main cause of neonatal septicaemia and meningitis, which is associated with high morbidity and mortality.

Treatment

Screening mothers in late pregnancy for carriage of GBS is now widespread practice in Australia. If the mother tests positive for GBS, antimicrobials are administered to her during delivery to prevent transmission to the baby, regardless of the delivery mode. Benzylpenicillin is the recommended agent for this purpose; cefazolin or lincomycin/clindamycin are recommended for

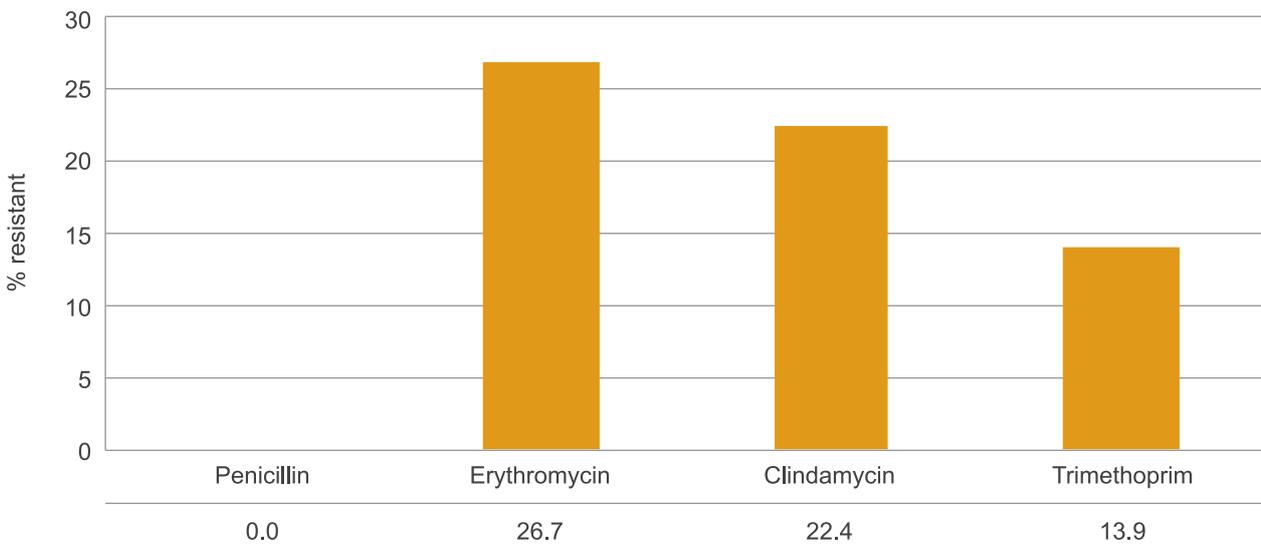
women with penicillin allergy, depending on the type and severity of the allergy.

Types and impact of resistance

Resistance to benzylpenicillin and cefazolin is emerging but still uncommon in Australia, but resistance to erythromycin, lincomycin and clindamycin is common, at around 20%. Resistance to lincomycin and clindamycin is strongly linked to resistance to macrolides such as erythromycin, which is often used in the laboratory as the test agent to predict resistance to lincomycin and clindamycin. Mothers who carry GBS that is resistant to erythromycin, lincomycin and clindamycin, but who would otherwise be treated with lincomycin or clindamycin, require prophylaxis with vancomycin.

Key findings: national

Resistance to benzylpenicillin was not found, but resistance to erythromycin and clindamycin exceeded 20% (Figure 4.39). This is important because an erythromycin resistance rate of 20% is the threshold at which protocols may need to be reconsidered and alternative agents used.

Figure 4.39: *Streptococcus agalactiae* resistance to individual agents, 2015

Note: $n = 5,175$

Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

Resistance to benzylpenicillin was not found in S. agalactiae, but resistance to erythromycin and clindamycin exceeded 20%.

4.13 *Streptococcus pneumoniae*

This section describes the health impact, treatment, types and impact of resistance, and key findings for resistance rates in *S. pneumoniae*.

Health impact

S. pneumoniae is an important pathogen that commonly causes acute otitis media, acute sinusitis and pneumonia. It can also cause septicaemia (especially in young children) and bacterial meningitis. Its capacity to cause disease is linked to its polysaccharide capsule, of which there are more than 90 serotypes.

In Australia, two pneumococcal vaccines are included in the National Immunisation Program. Infants receive a conjugated vaccine that covers

13 of the most common serotypes, and older people and those with risk factors receive a polysaccharide vaccine that covers 23 of the most common serotypes. Because of the incomplete coverage of all serotypes, not all pneumococcal infection is vaccine preventable.

Treatment

Otitis media and sinusitis are normally treated with oral amoxicillin, cefuroxime (in penicillin-allergic patients) or doxycycline (for people older than 8 years). Macrolides and trimethoprim-sulfamethoxazole are sometimes used for oral treatments. Pneumonia and meningitis are generally treated with benzylpenicillin if the strain is proven to be susceptible, or ceftriaxone (or cefotaxime) for penicillin-nonsusceptible strains. Strains causing pneumonia or meningitis that are non-susceptible to penicillin and ceftriaxone (rare) require treatment with reserve antimicrobials, such as vancomycin or meropenem.

Types and impact of resistance

Reduced susceptibility to benzylpenicillin is common but can mostly be managed with increased dosing regimens of benzylpenicillin, or amoxicillin when oral treatment is appropriate. However, strains with reduced susceptibility causing meningitis are resistant to treatment with benzylpenicillin as a result of the relatively poor penetration of this antimicrobial into the subarachnoid space (where the infection is located). Meningitis caused by these strains requires treatment with ceftriaxone or cefotaxime, unless the strains also have reduced susceptibility to these agents.

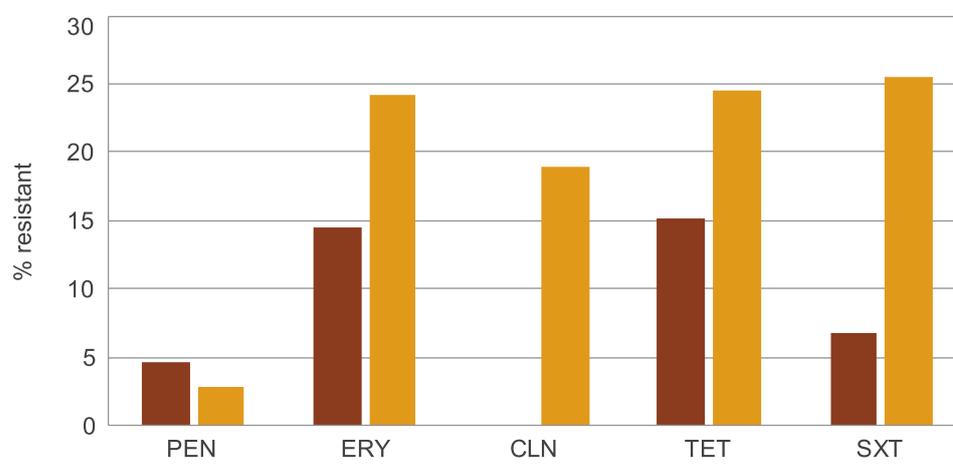
Resistance to tetracycline predicts resistance to doxycycline, the usual agent in this class used for treatment in adolescents and adults, and is a feature of multidrug-resistant strains.

Key findings: national

Resistance to benzylpenicillin was low, but rates of resistance to macrolides (erythromycin), tetracycline and trimethoprim-sulfamethoxazole were all above 20% for specimens other than blood (Figure 4.40). Rates of resistance were somewhat lower for blood isolates than for isolates from other specimens. There were no major differences in resistance rates in different clinical settings (Figure 4.41).

S. pneumoniae resistance to benzylpenicillin was low, but rates of resistance to erythromycin, tetracycline and trimethoprim-sulfamethoxazole were all above 20%.

Figure 4.40: *Streptococcus pneumoniae* resistance to individual agents used in treatment, by specimen source, 2015

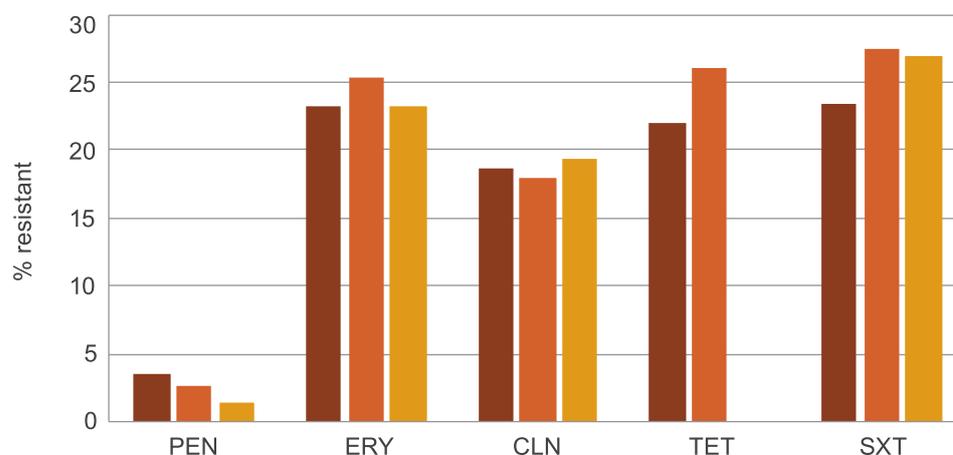


■ Blood (n = 324)	4.6	14.5	–	15.1	6.7
■ Other (n = 3,938)	2.8	24.1	18.9	24.4	25.5

– = not available (either not tested or tested against an inadequate number of isolates); CLN = clindamycin; ERY = erythromycin; PEN = benzylpenicillin; SXT = trimethoprim-sulfamethoxazole; TET = tetracycline

Note: Benzylpenicillin resistance is defined as a minimum inhibitory concentration of >2 mg/L (infections other than meningitis) by the European Committee on Antimicrobial Susceptibility Testing.

Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

Figure 4.41: *Streptococcus pneumoniae* resistance, by clinical setting, 2015

	PEN	ERY	CLN	TET	SXT
Public hospitals (n = 2,662)	3.6	23.3	18.8	22.1	23.5
Private hospitals (n = 536)	2.8	25.4	18.1	26.2	27.5
Community (n = 1,209)	1.5	23.3	19.4	–	26.9

– = not available (either not tested or tested against an inadequate number of isolates); CLN = clindamycin; ERY = erythromycin; PEN = benzylpenicillin; SXT = trimethoprim-sulfamethoxazole; TET = tetracycline

Note: Benzylpenicillin resistance is defined as a minimum inhibitory concentration of >2 mg/L (infections other than meningitis) by the European Committee on Antimicrobial Susceptibility Testing.

Sources: AGAR and National Passive AMR Surveillance System (OrgTRx) (public hospitals); AGAR, OrgTRx (SA) and SNP (private hospitals); OrgTRx (SA) and SNP (community)

4.14 *Streptococcus pyogenes*

This section describes the health impact, treatment, types and impact of resistance, and key findings for resistance rates in *S. pyogenes*.

Health impact

S. pyogenes, also called group A *Streptococcus*, is an important human pathogen. It most commonly causes skin and soft tissue infections, and acute pharyngitis, but can cause serious and life-threatening infections such as scarlet fever, septicaemia, bone and joint infections, toxic shock syndrome, necrotising fasciitis and pneumonia. This organism is also associated with two 'post-streptococcal' syndromes: acute glomerulonephritis and rheumatic fever. These syndromes are now rare in most parts of Australia, but are still seen frequently in remote Aboriginal and Torres Strait Islander communities, contributing to substantial long-term morbidity in these populations.

Treatment

Benzylpenicillin remains the treatment of choice for *S. pyogenes* infections. In patients who are allergic to penicillins, macrolides such as erythromycin and first-generation cephalosporins are treatment options. Patients who have experienced one episode of acute rheumatic fever are prone to further episodes and worsening organ damage; as a consequence, they are administered long-term prophylaxis (usually over decades) with benzathine penicillin (intramuscularly) or phenoxymethylpenicillin (orally).

Types and impact of resistance

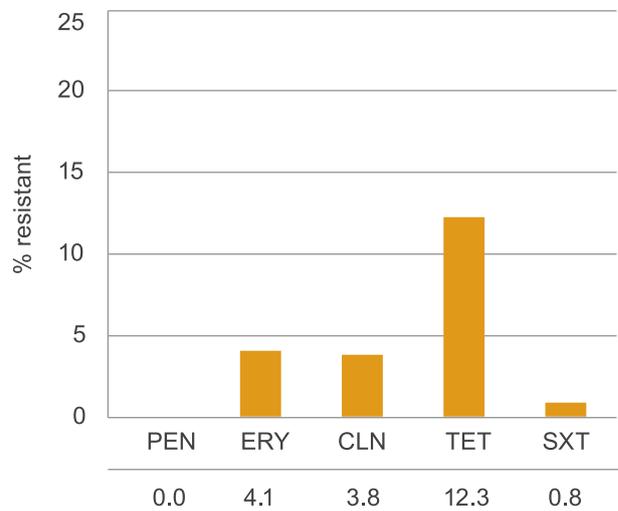
Confirmed resistance to benzylpenicillin has never been reported anywhere in the world in this species, but the consequences of its emergence would be substantial. It is expected that, based on observations of other species of *Streptococcus*, resistance to benzylpenicillin would also affect susceptibility to first-generation cephalosporins. In contrast, acquired resistance to macrolide antimicrobials has been present in *S. pyogenes* for many years. Levels of resistance seem to fluctuate in line with changes in circulating clones.

Key findings: national

Resistance to key antimicrobial agents was low, apart from tetracyclines, which are rarely used for treatment (Figure 4.42). Resistance to erythromycin (and therefore other macrolides) was low. There was some variation in macrolide resistance rates among clinical settings (Figure 4.43).

Resistance to key antimicrobial agents in S. pyogenes was low, apart from tetracyclines, which are rarely used for treatment.

Figure 4.42: *Streptococcus pyogenes* resistance to individual agents (all sources), 2015



CLN = clindamycin; ERY = erythromycin; PEN = benzylpenicillin; SXT = trimethoprim-sulfamethoxazole; TET = tetracycline
 Note: n = 14,172

Sources: AGAR (national); National Passive AMR Surveillance System (OrgTRx) (ACT, NSW, Qld, SA, Tas, Vic); SNP (Qld and northern NSW)

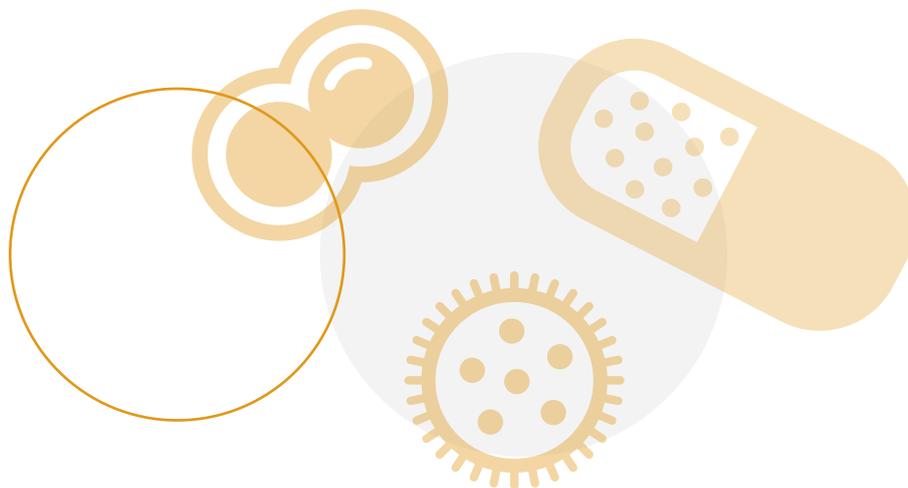
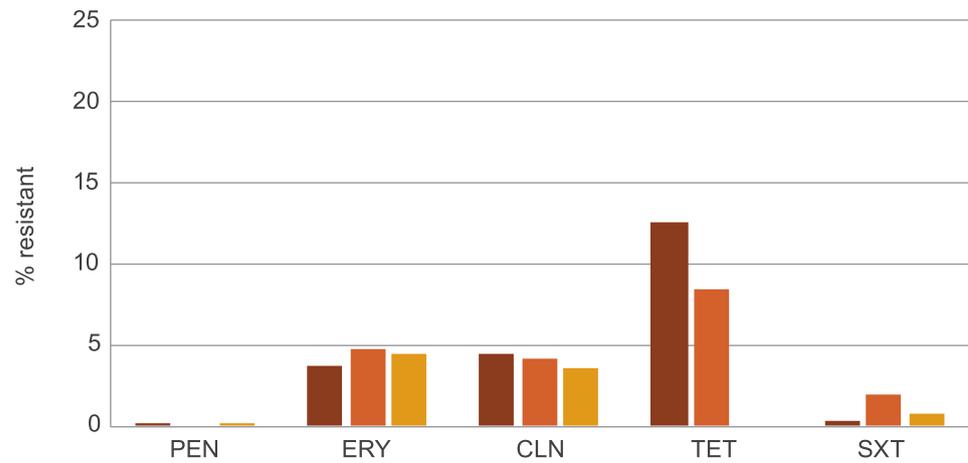


Figure 4.43: *Streptococcus pyogenes* resistance, by clinical setting, 2015

	PEN	ERY	CLN	TET	SXT
Public hospitals (n = 7,420)	0.0	3.7	4.5	12.6	0.3
Private hospitals (n = 1,776)	0.0	4.7	4.2	8.4	2.0
Community (n = 4,981)	0.0	4.5	3.6	–	0.8

– = not available (either not tested or tested against an inadequate number of isolates); CLN = clindamycin; ERY = erythromycin; PEN = benzylpenicillin; SXT = trimethoprim-sulfamethoxazole; TET = tetracycline

Sources: AGAR and National Passive AMR Surveillance System (OrgTRx) (public hospitals); AGAR, OrgTRx (SA) and SNP (private hospitals); OrgTRx (SA) and SNP (community)

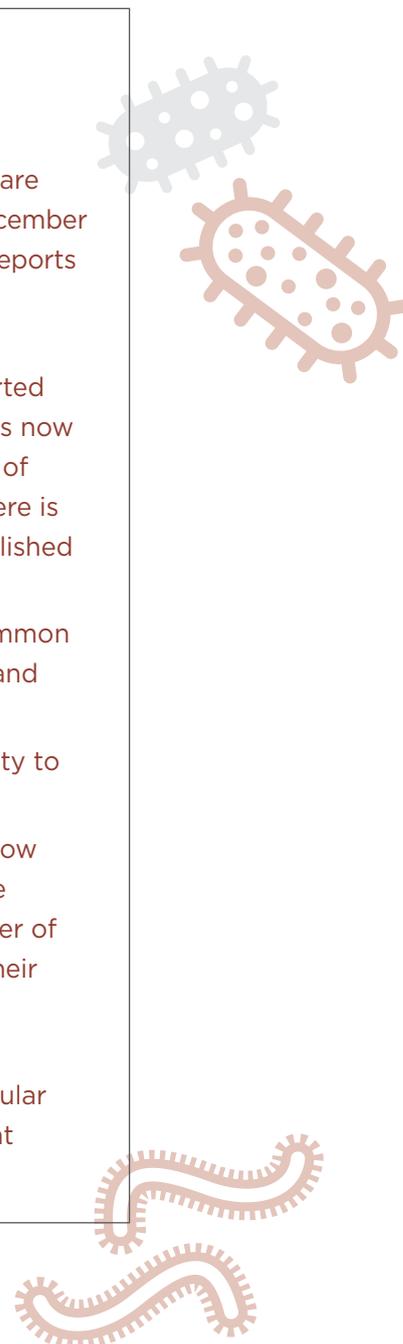


Chapter 5

National Alert System for Critical Antimicrobial Resistances (CARAlert)

Key messages

- The National Alert System for Critical Antimicrobial Resistances (CARAlert) collects surveillance data on priority organisms that are resistant to last-line antimicrobial agents. From 17 March to 31 December 2016, 673 results were submitted to CARAlert; isolates for these reports were referred from 70 originating laboratories across Australia.
- Carbapenemase-producing Enterobacteriaceae were the most frequently recorded critical antimicrobial resistance (CAR) reported to date (48% of CARs reported). The IMP-type carbapenemase is now endemic on the Australian eastern seaboard, in multiple species of Enterobacteriaceae (most commonly *Enterobacter cloacae*). There is no evidence yet that other carbapenemases have become established in Australia.
- Azithromycin-nonsusceptible *Neisseria gonorrhoeae* is more common in Australia than originally thought, and seems to be spreading and appearing in different states at different times.
- No reports of *Streptococcus pyogenes* with reduced susceptibility to penicillin were submitted to the system in 2016.
- The number of records in the database to date is too small to allow specific conclusions to be drawn from the analyses; however, the data undergo regular epidemiological analysis, and as the number of reports increases to enable meaningful analyses of trends and their implications, these aspects will also be reported on.
- The Australian Commission on Safety and Quality in Health Care will continue to monitor records from CARAlert and prepare regular summary reports. CARAlert data will inform quality improvement initiatives and policies to reduce antimicrobial resistance.



This chapter summarises the results of the first nine months of operation of the National Alert System for Critical Antimicrobial Resistances (CARAlert): 17 March to 31 December 2016.

5.1 Overview of the CARAlert system

CARAlert was established by the Australian Commission on Safety and Quality in Health Care (the Commission) in March 2016 as an integral component of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System, to further strengthen surveillance of antimicrobial resistance.

CARAlert collects data on nationally agreed priority organisms that are resistant to last-line antimicrobial agents, and known as critical antimicrobial resistances (CARs; Table 5.1). CARs are resistance mechanisms, or resistance profiles, that are known to be a serious threat to the effectiveness of last-line antimicrobial agents. CARs have been detected across Australia. They

may result in significant morbidity and mortality in healthcare facilities and in the community.

CARs are resistance mechanisms, or resistance profiles, that are known to be a serious threat to the effectiveness of last-line antimicrobial agents.

The Commission established CARAlert to provide more timely advice to state and territory health authorities on the occurrence of CARs in their hospitals and communities, to provide a national picture of these CARs, and to complement the existing processes for confirming CARs.

Although some data on CARs are captured through existing surveillance programs, the CARAlert system is the first nationally coordinated system that supports both collection and communication of information on confirmed CARs and potential CAR outbreaks, as close as possible to the time of confirmation.

Table 5.1: Critical antimicrobial resistances included in CARAlert

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

CARAlert processes

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

1. Collection and routine testing – the isolate is collected from the patient and sent to the originating laboratory for routine testing
2. 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
3. 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 details of the resistance and the organism into the secure CARAlert web portal.

Public and private pathology laboratories that have the capacity to confirm CARs were identified through consultation with state and territory health authorities, the Public Health Laboratory Network and the Australian Group on Antimicrobial Resistance. There are currently 28 confirming laboratories participating in CARAlert.

CARAlert generates a weekly summary email alert to report information on confirmed CARs to state and territory health authorities, and the Australian Government Department of Health. The information collected through CARAlert allows health service providers, laboratories, public health units and policymakers at local, state and territory, and national levels to receive timely reports and analyses of national data, which complement current local reporting to the providers of patient care. In addition, regular summary reports are made available on the Commission's website.

CARAlert generates a weekly summary email alert to report information on confirmed CARs to state and territory health authorities, and the Australian Government Department of Health.

Since October 2016, secure access to the CARAlert system has provided state and territory health authorities with access to the name of the public hospital where the patient who had the infection was being cared for at the time the specimen was collected. This enables them to monitor the geographic distribution of CARs, and to liaise with hospitals, as appropriate, to confirm that infection control action has been taken in the event of an outbreak. These authorities can also generate their own reports from CARAlert. Over time, the data will become increasingly useful to inform a broader range of safety and quality improvement programs. No patient-level data are held by the CARAlert system.

It is intended that states and territories will use the data to identify local issues, and respond to potential and proven multi-site outbreaks of CARs. Primary responsibility for clinical response to CARs lies with local health organisations, and state and territory health departments.

The organisms reported under CARAlert are drawn from the list of high-priority organisms and antimicrobials that are the focus of the AURA Surveillance System. The scope of organisms and CARs are regularly reviewed, based on the latest evidence on CARs that emerge in Australia and overseas. The most recent review, in October 2016, did not result in any changes to the list.

5.2 Results from CARAlert 2016

Information in this chapter relates to CARs that were submitted to the CARAlert system between 17 March 2016 and 31 December 2016. Data for most CARs are reported by the date that the CAR was confirmed, not the date it was submitted to CARAlert. Generally, CARs are submitted to CARAlert within seven days of the isolate being confirmed as a CAR. However, the results are provided to the originating laboratory as soon as possible after confirmation.

Isolates of *Neisseria gonorrhoeae* that were referred to the National Neisseria Network are reported by both date of collection and date of more extensive testing being completed by the confirming laboratory. The confirming laboratories often conduct batch testing, so results may not be finalised or submitted until the following months. However, the originating laboratory provides all results of its testing back to the referrer so that timely treatment can begin.

Critical antimicrobial resistance overall

Between 17 March and 31 December 2016, 673 results from 70 originating laboratories across Australia were entered into CARAlert. From April 2016, there was an average of 71 entries per month (range 61-82). The proportion of CARs associated with priority organisms each month is shown in Figure 5.1.

Between 17 March and 31 December 2016, 673 results from 70 originating laboratories across Australia were entered into CARAlert.

Carbapenemase-producing Enterobacteriaceae (CPE) were the most frequently recorded CAR ($n = 326$; 48%), either alone (305; 45%) or in combination with production of ribosomal

methyltransferases (21; 3%). Differences in the proportions of CPE recorded per month were not statistically significant (χ^2 for trend, $P = 0.0502$) (Figure 5.2).

The next most frequently reported CAR was azithromycin-nonsusceptible *N. gonorrhoeae* ($n = 209$; 31%). This CAR is often confirmed in batches, which influences the numbers reported per month. Only four of the 209 (2%) azithromycin-resistant *N. gonorrhoeae* were reported to have high-level resistance (HLR) – that is, a minimum inhibitory concentration (MIC) ≥ 256 mg/L. There was a significant increase in the proportion of *N. gonorrhoeae* per month (χ^2 for trend, $P = 0.0194$) (Figure 5.2).

Carbapenemase-producing Enterobacteriaceae were the most frequently recorded CAR, followed by azithromycin-nonsusceptible Neisseria gonorrhoeae.

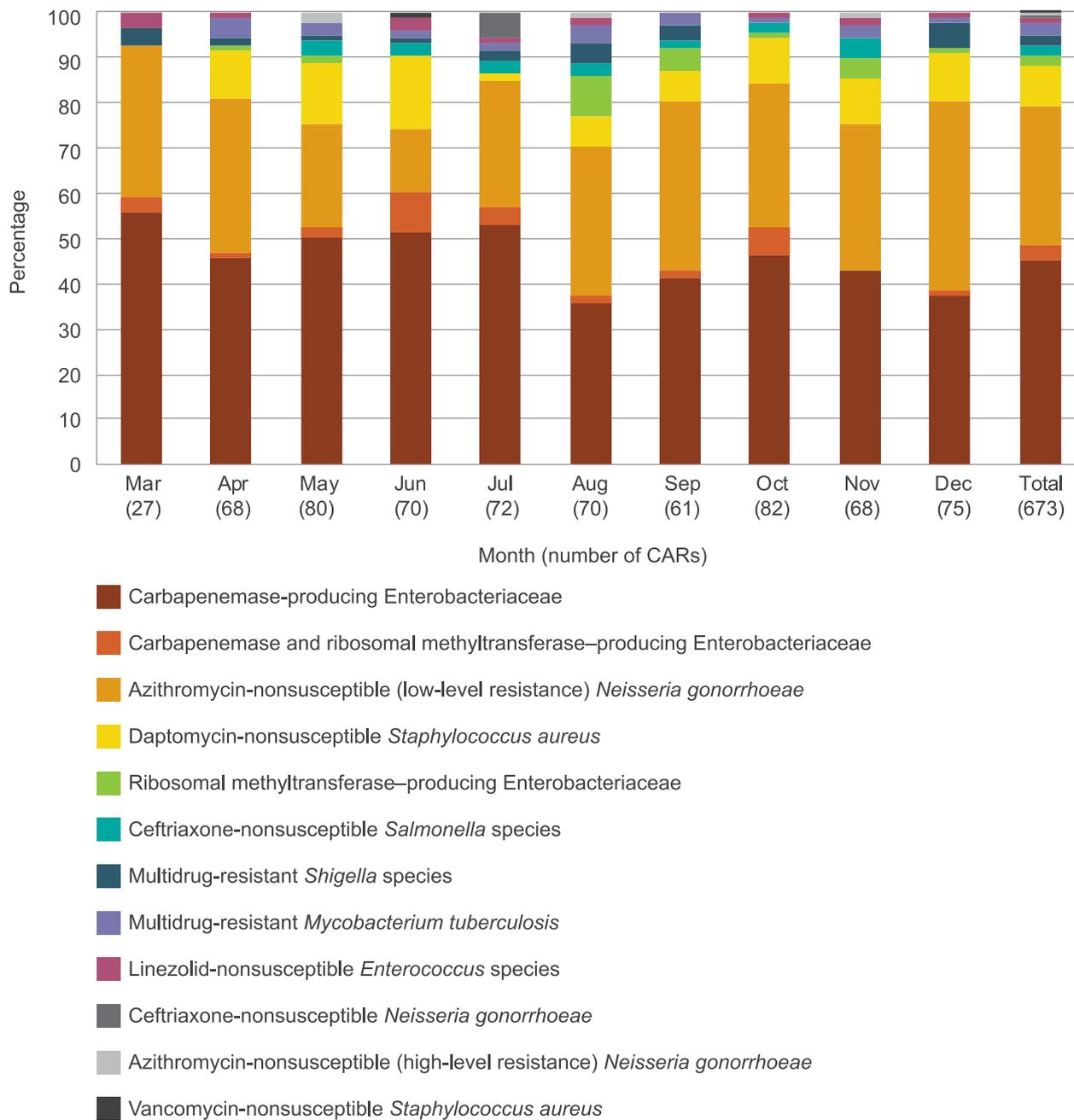
Critical antimicrobial resistances by state and territory

Most CARs (74%) were collected from patients who lived in the three most populous states: New South Wales (34%), Victoria (22%) and Queensland (18%). Only one submission was received from the Northern Territory, and five were from Tasmania. CPE as a proportion of all reported CARs was lowest in Western Australia (28%) and South Australia (32%), and highest in Queensland (73%) (Figure 5.3).

Most CARs (74%) were collected from patients who lived in the three most populous states: New South Wales (34%), Victoria (22%) and Queensland (18%).



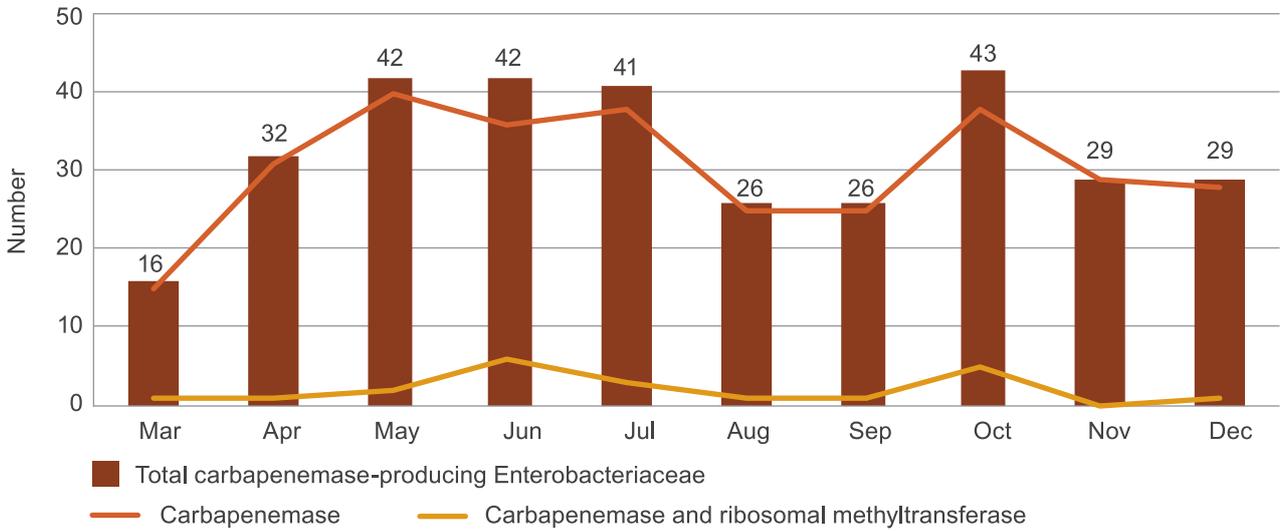
Figure 5.1: Critical antimicrobial resistances reported, by month of confirmation, 17 March - 31 December 2016



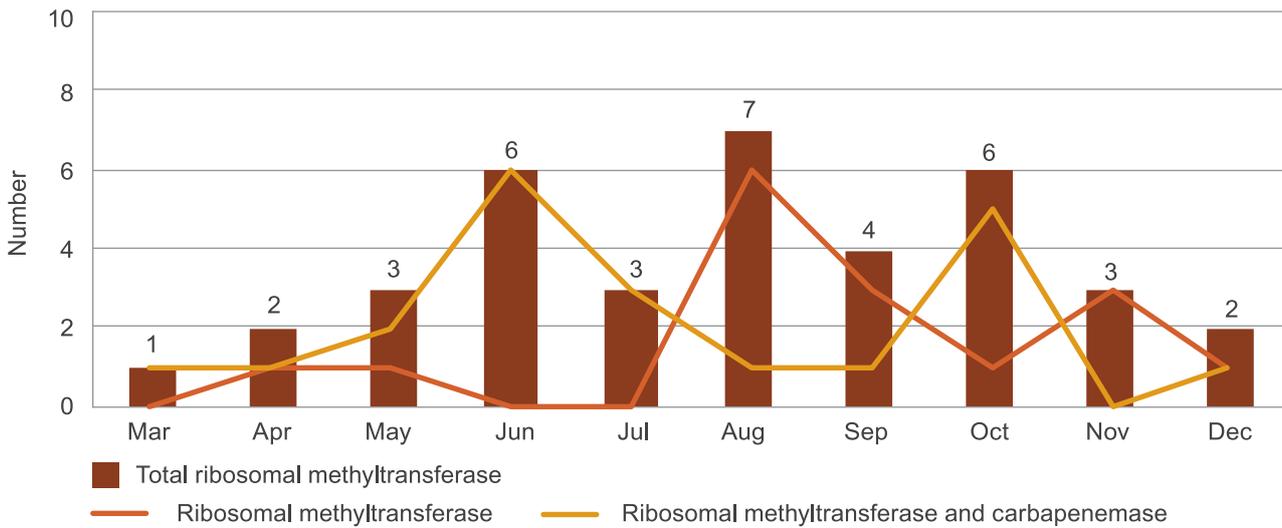
Note: Low-level resistance is a minimum inhibitory concentration (MIC) <256 mg/L. High-level resistance is an MIC ≥256 mg/L.
Source: CARAlert

Figure 5.2: Number of critical antimicrobial resistances reported, by organism and month of confirmation, 17 March - 31 December 2016

Enterobacteriaceae – carbapenemase producing



Enterobacteriaceae – ribosomal methyltransferase producing



Neisseria gonorrhoeae

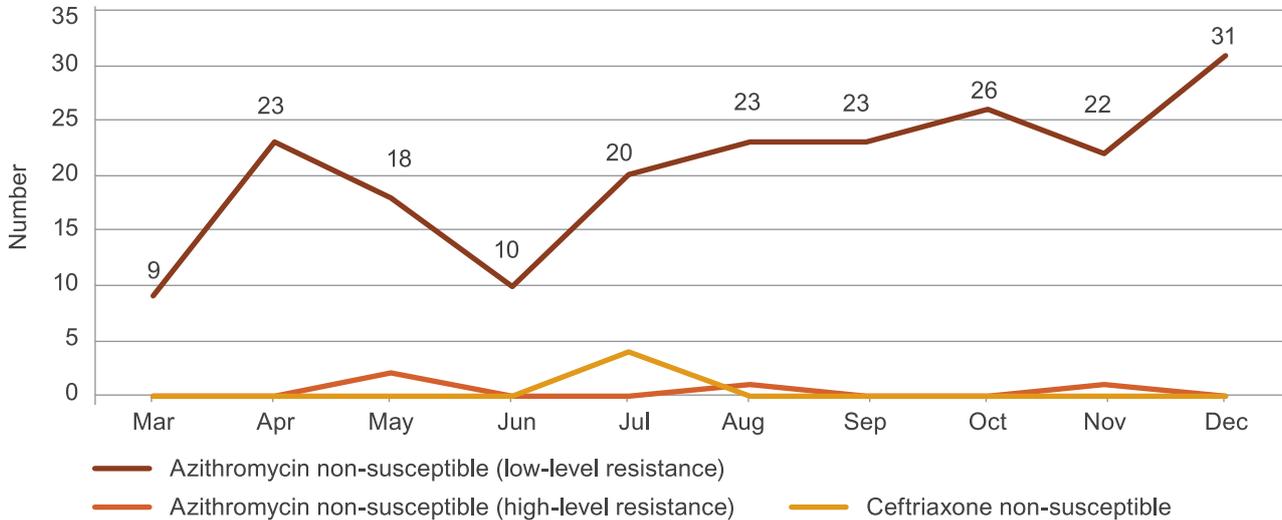
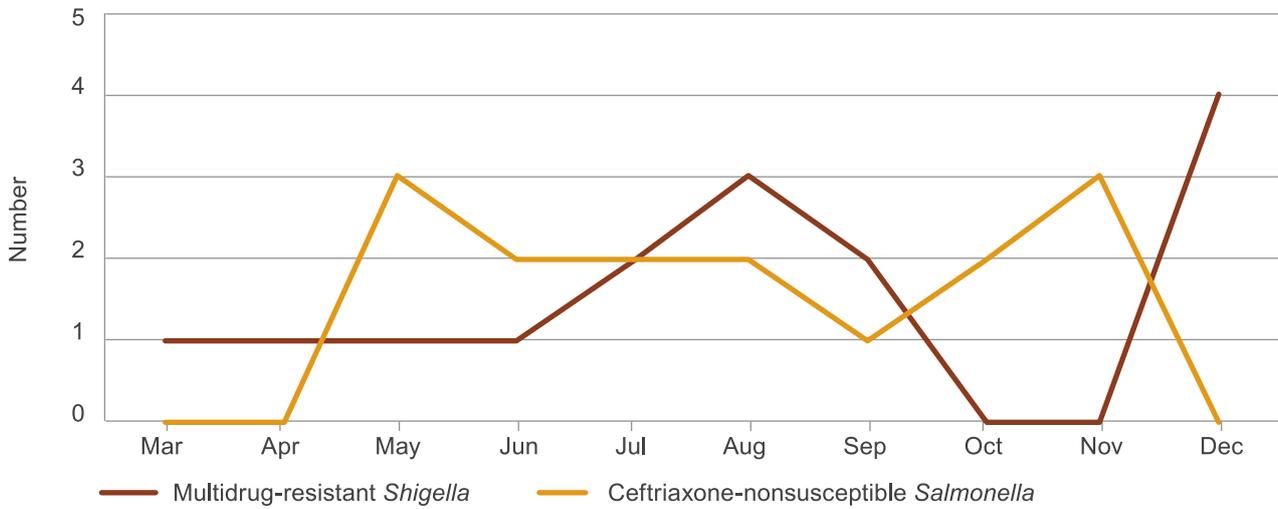


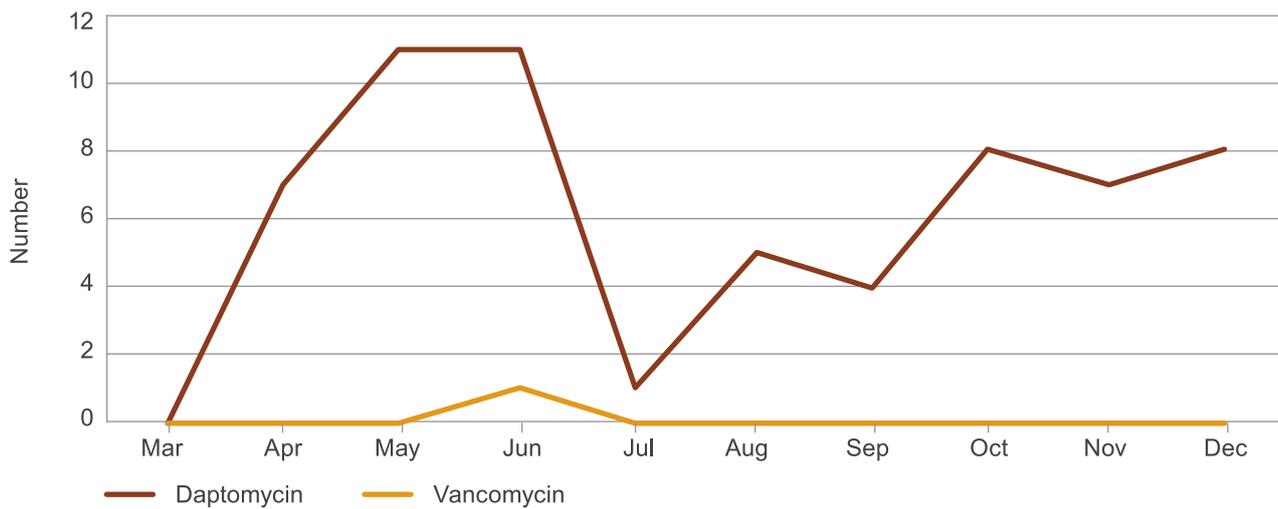


Figure 5.2: continued

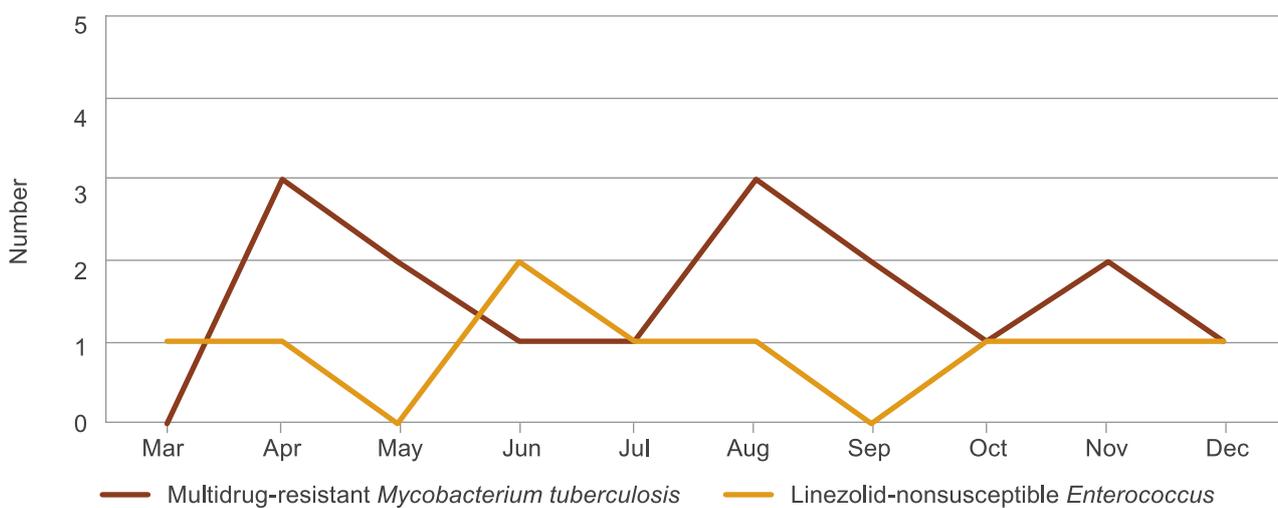
Salmonella and *Shigella* species



Staphylococcus aureus

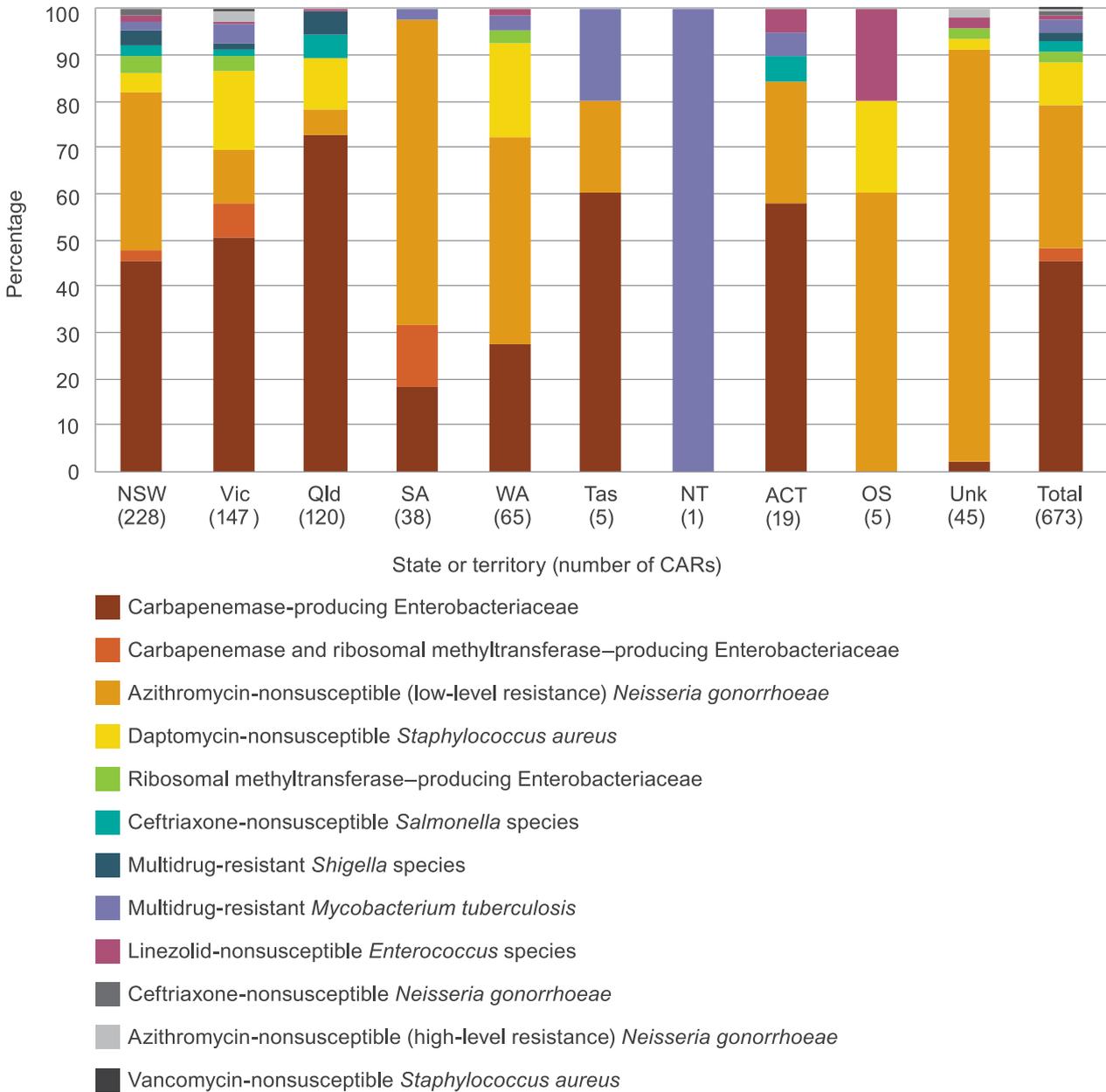


Enterococcus species and *Mycobacterium tuberculosis*



Source: CARAlert

Figure 5.3: Critical antimicrobial resistances (CARs), by patient’s state or territory of residence, 17 March – 31 December 2016



OS = overseas; Unk = unknown

Note: Low-level resistance is a minimum inhibitory concentration (MIC) of <256 mg/L. High-level resistance is an MIC of ≥256 mg/L.

Source: CARAlert



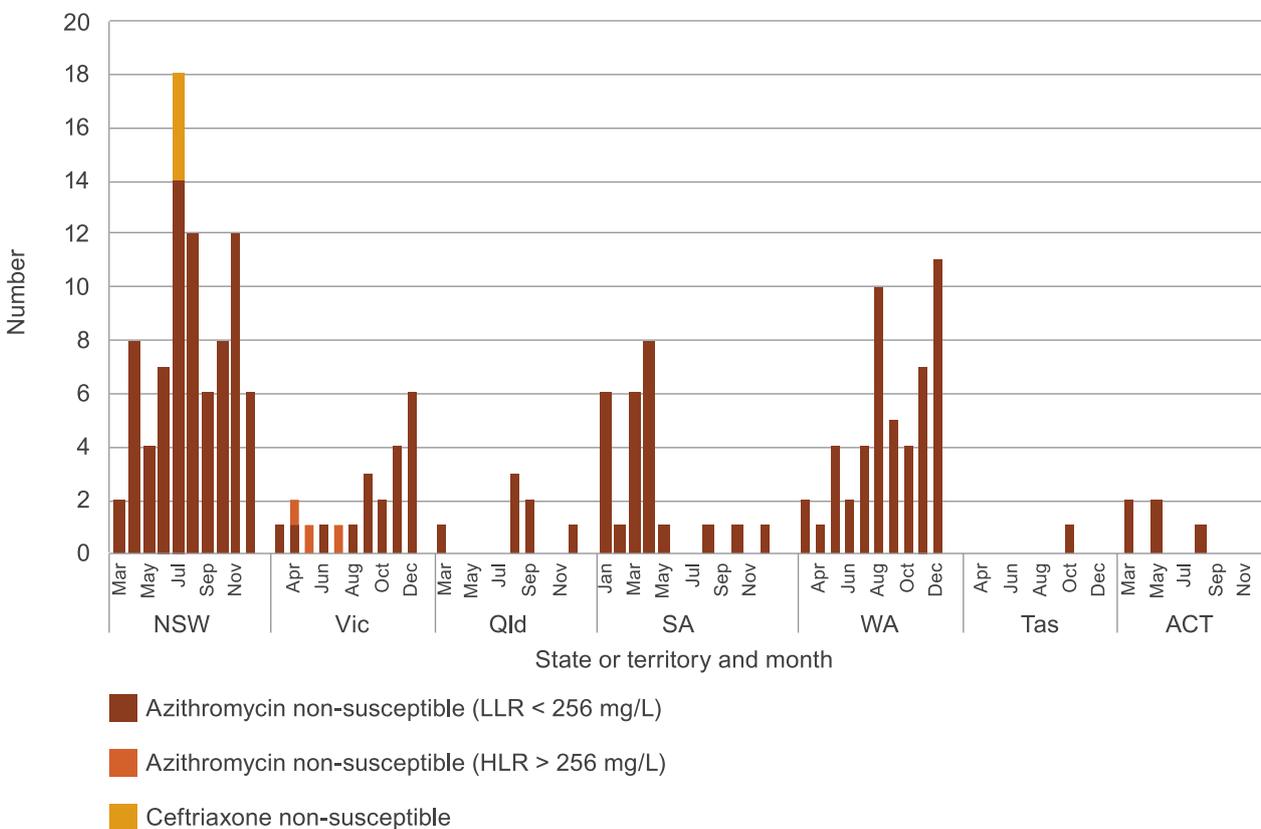
State or territory of residence was not available for 45 submissions: 40 azithromycin-resistant (low-level resistance [LLR], MIC <256 mg/L) *N. gonorrhoeae*; one CPE; one ribosomal methyltransferase-producing Enterobacteriaceae; one azithromycin-resistant (HLR, MIC \geq 256 mg/mL) *N. gonorrhoeae*; one linezolid-nonsusceptible *Enterococcus* species; and one daptomycin-nonsusceptible *Staphylococcus aureus*. For *N. gonorrhoeae*, this is because the isolates were collected from sexual health clinics, where postcode of residence is not always sought.

Five submissions were from overseas residents: one daptomycin-nonsusceptible *S. aureus*, one linezolid-nonsusceptible *Enterococcus* species, and three azithromycin-resistant (LLR, MIC <256 mg/L) *N. gonorrhoeae*.

Daptomycin-nonsusceptible *S. aureus* was reported from four states and territories; 40% (25/62) of these were from Victoria, 21% (13/62) were from Queensland, 21% (13/62) were from Western Australia, and 15% (9/62) were from New South Wales. Multidrug-resistant *Mycobacterium tuberculosis* was reported from patients from all states and territories except Queensland.

There was a relatively large number of submissions of azithromycin-nonsusceptible (LLR, MIC <256 mg/L) *N. gonorrhoeae* from South Australia in March 2016. As batch testing of this CAR is common, reports were analysed by date of collection, rather than date of confirmation (Figure 5.4). Isolates with LLR from South Australia were collected in January 2016, and only small numbers of strains were confirmed with a collection date after April 2016. There was

Figure 5.4: Critical antimicrobial resistances, *Neisseria gonorrhoeae*, number reported by state and territory of residence, by month of collection, 2016



HLR = high-level resistance; LLR = low-level resistance

Source: CARAlert

a subsequent sharp increase in submissions of this CAR, with a peak in July 2016 from New South Wales. Although the number of LLR submissions has declined in several states and territories, both Western Australia and Victoria reported significant increases from August (Western Australia) and September (Victoria) to December 2016. Four strains with azithromycin HLR (MIC \geq 256 mg/L) were confirmed: three from Victoria (collected in April, May and July 2016), and one in October 2016 from an unknown place of residence, but originating from South Australia. Ceftriaxone-nonsusceptible strains collected in July 2016 were also confirmed from New South Wales.

Critical antimicrobial resistances by age group

CARs were isolated from patients of all ages, from birth to >80 years, with a median age of 50–59 years (Figure 5.5). Seventy per cent (228/326) of CPE were isolated from people aged 60 years and older. Azithromycin-resistant *N. gonorrhoeae* was the predominant CAR reported among the age groups of 15–19, 20–29, 30–39 and 40–49. Only 3% (21/673) of all CARs were reported in children aged less than 15 years; CPE and ceftriaxone-nonsusceptible *Salmonella* species were common (76%) in this age group.

Seventy per cent of CPE were isolated from people aged 60 years and older. Azithromycin-resistant N. gonorrhoeae was the predominant CAR reported among people aged 15–49.

Critical antimicrobial resistances by specimen type

More than 76% 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 5.6).

Fifty-eight per cent (189/326) of CPE isolates were from clinical specimens; 61% (115/189) of these were from urine, and 10% (18/189) were from blood cultures. One linezolid-nonsusceptible *Enterococcus faecalis* and one daptomycin-nonsusceptible *S. aureus* were from blood culture. Urine is an important specimen for certain CARs, such as CPE, because the urinary tract is a common site of infection.

Critical antimicrobial resistances by facility type

Most CARs (61%; 408/673) were detected in either hospitalised patients or hospital outpatients, but some were isolated in the community (24%; 162/673) and in aged care homes (Figure 5.7). Facility type for azithromycin-resistant *N. gonorrhoeae* was difficult to obtain because most isolates are referred to a public health laboratory for confirmation, and may therefore reflect the facility from which the isolate was sent rather than the facility that the patient attended.

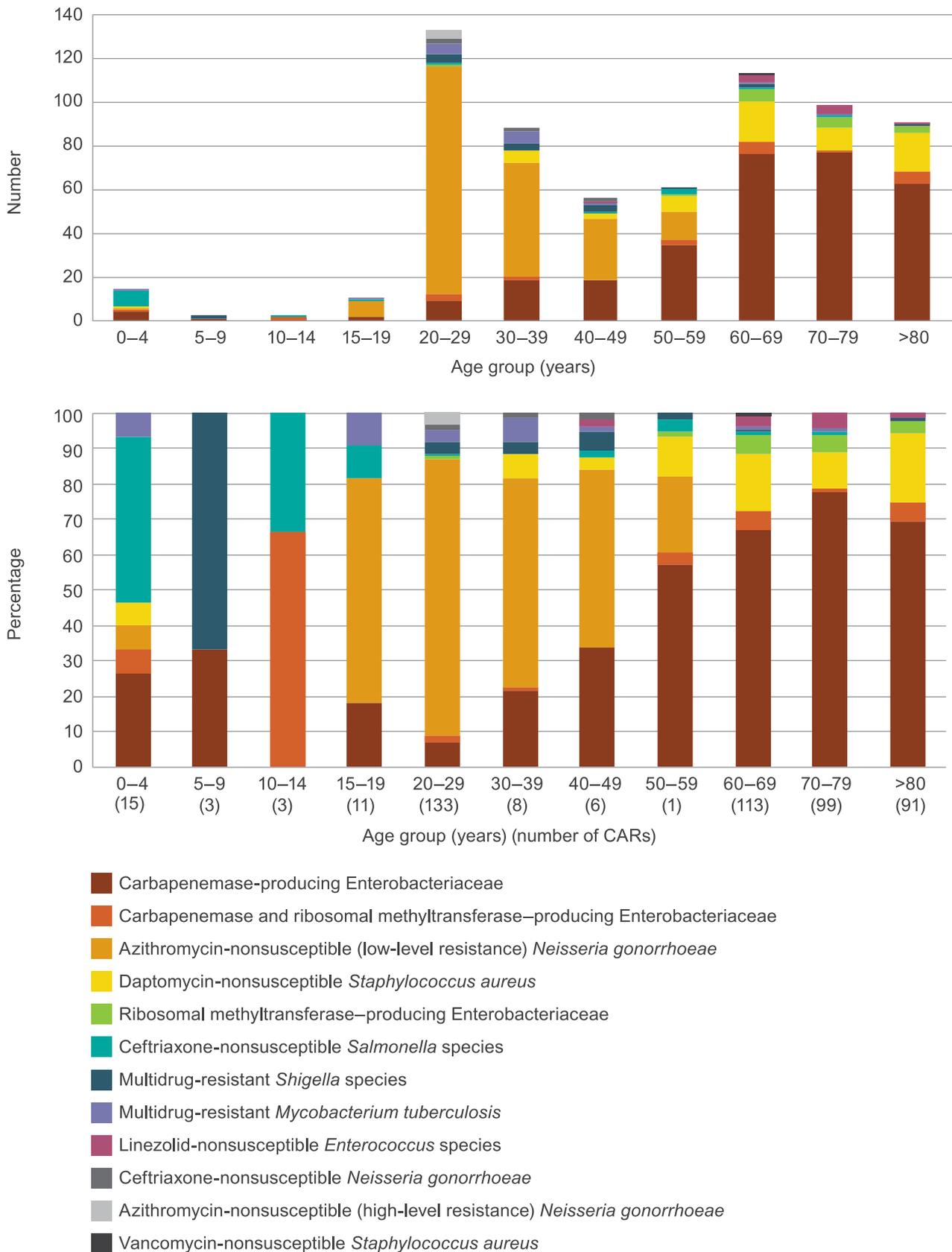
Most CARs were detected in either hospitalised patients or hospital outpatients, but some were isolated in the community and in aged care homes.

Carbapenemase-producing Enterobacteriaceae type by state and territory

Six different carbapenemase types (IMP, NDM, OXA-48-like, KPC, VIM and SME) were reported throughout Australia, with notable regional differences (Figure 5.8). Two carbapenemase types accounted for 84% of all Enterobacteriaceae with a confirmed carbapenemase: IMP (64%; 208/326) and NDM (20%; 65/326).

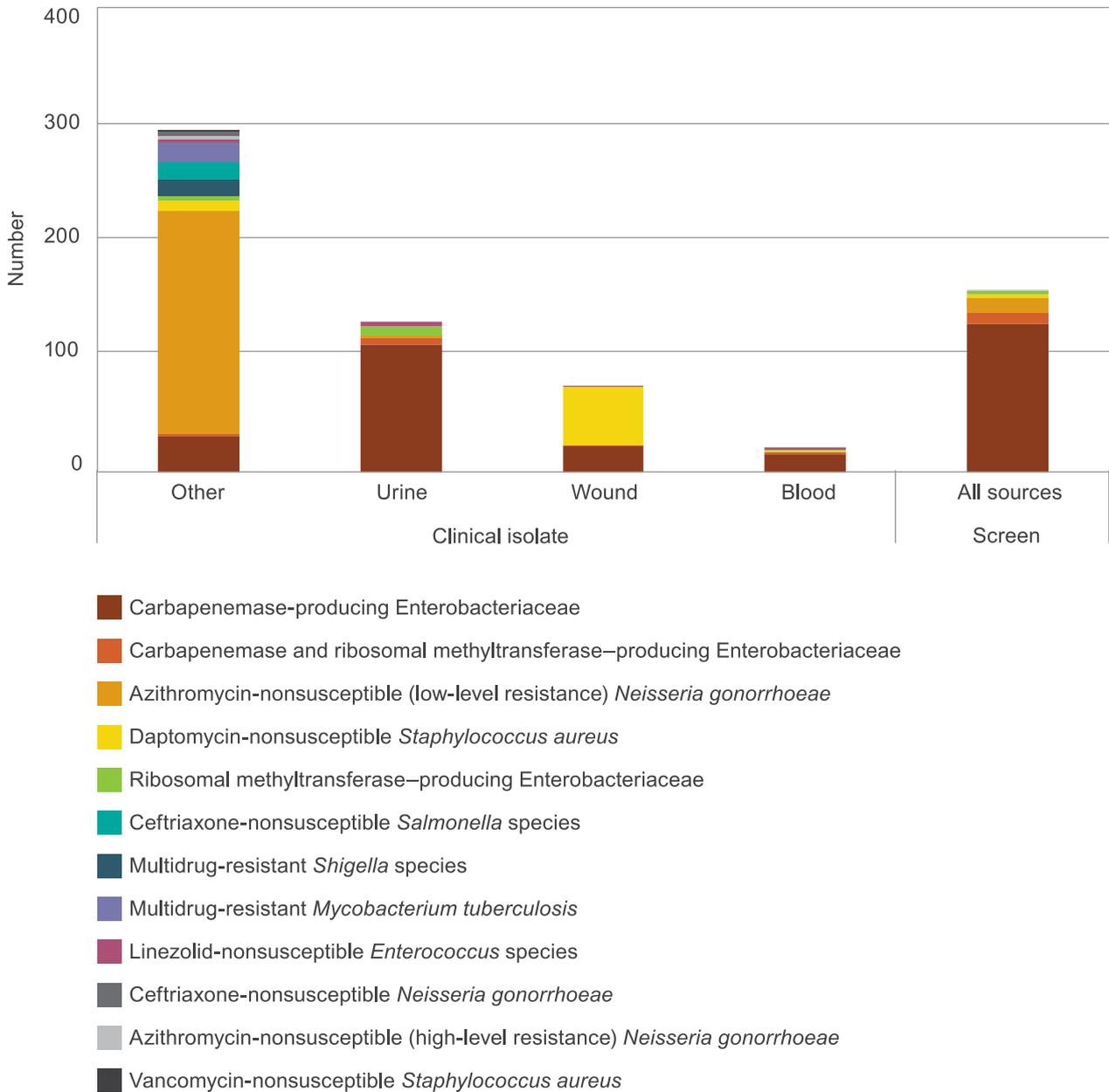


Figure 5.5: Critical antimicrobial resistances (CARs), by age group, 17 March – 31 December 2016



Note: Low-level resistance is a minimum inhibitory concentration (MIC) of <256 mg/L. High-level resistance is an MIC of ≥256 mg/L
Source: CARAlert

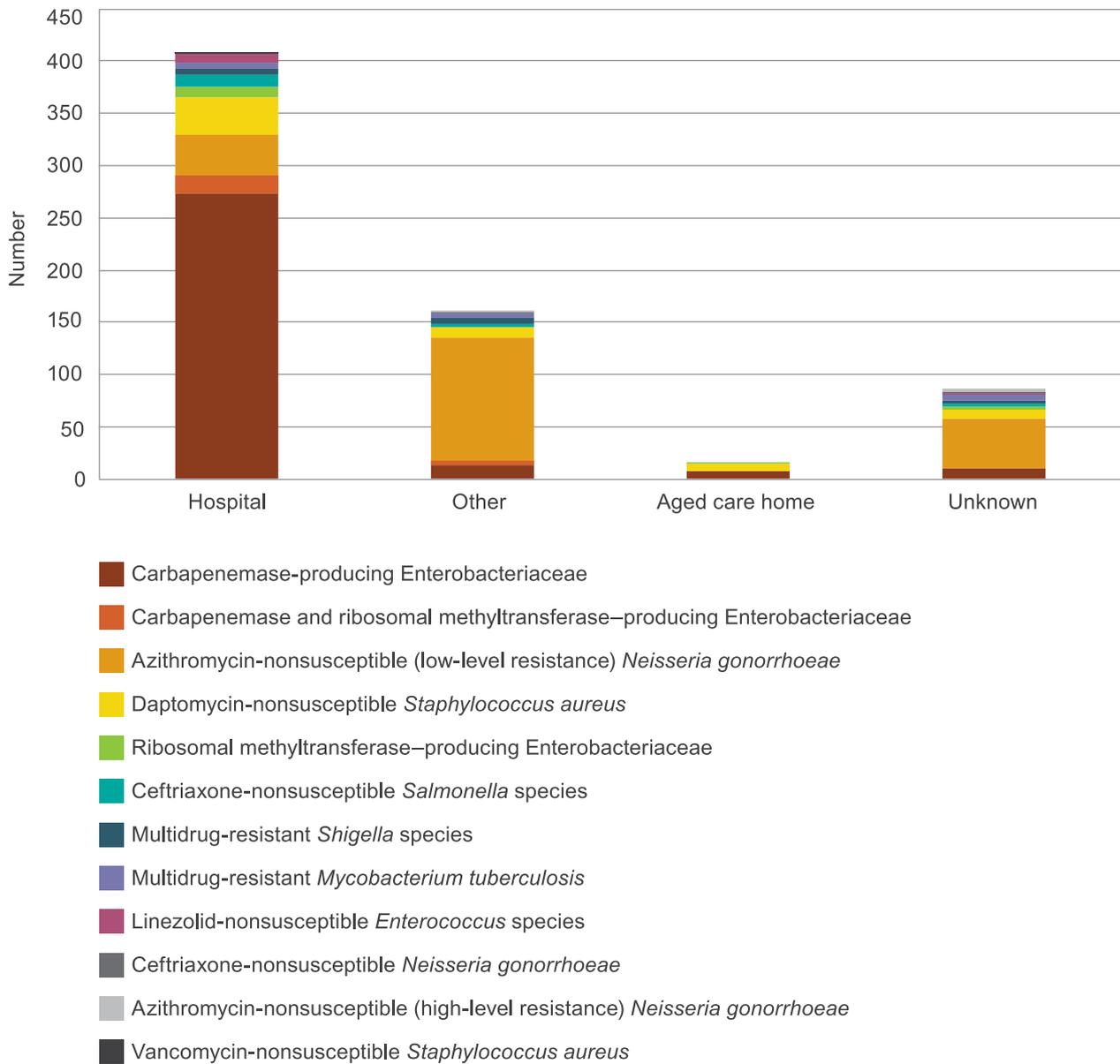
Figure 5.6: Critical antimicrobial resistances reported, by specimen type, 17 March - 31 December 2016



Notes:

1. Low-level resistance is a minimum inhibitory concentration (MIC) of <256 mg/L. High-level resistance is an MIC of ≥256 mg/L.
2. 'Other' refers to specimen types other than urine, wound or blood, such as genital, faecal or respiratory tract.

Source: CARAlert

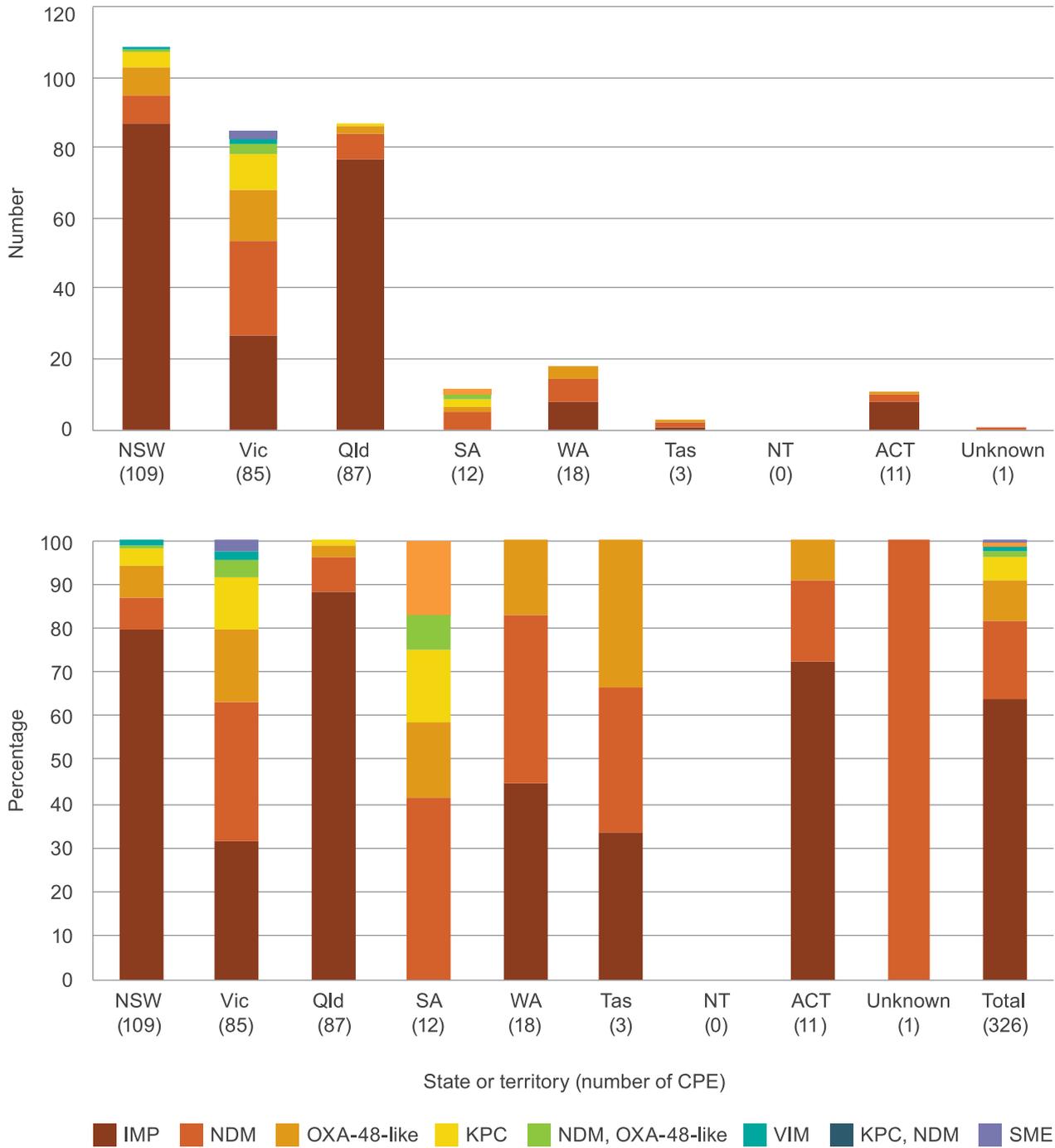
Figure 5.7: Critical antimicrobial resistances reported, by facility type, 17 March – 31 December 2016

Notes:

1. Low-level resistance is a minimum inhibitory concentration (MIC) of <256 mg/L. High-level resistance is an MIC of ≥256 mg/L.
2. 'Other' refers to community (non-hospital and non-aged care home).

Source: CARAlert

Figure 5.8: Carbapenemases produced by reported carbapenemase-producing Enterobacteriaceae (CPE), by patient's state or territory of residence; 17 March – 31 December 2016



Source: CARAlert

Six different carbapenemase types were reported throughout Australia, with notable regional differences.

IMP-type carbapenemases comprised the majority (>70%) of CPE in New South Wales (80%; 87/109), Queensland (89%; 77/87) and the Australian Capital Territory (73%; 8/11). No IMP-producing Enterobacteriaceae were reported from South Australia. All the strains that have been genetically sequenced to date (41%; 85/208) are *bla*IMP-4.

IMP-4-producing *Enterobacter cloacae* is endemic in mainland eastern states, but no evidence of outbreaks exists to date.

IMP-4-producing Enterobacter cloacae is endemic in mainland eastern states, but no evidence of outbreaks exists to date.

NDM types were found in all states and territories where CPE was detected. NDM + OXA-48-like (5/65) and NDM + *Klebsiella pneumoniae* carbapenemase (KPC) (2/65) were reported. Four different genes were found in the strains sequenced to date: *bla*NDM5 (39%; 14/36), *bla*NDM-1 (42%; 15/36), *bla*NDM-4 (11%; 4/36) and *bla*NDM-7 (8%; 3/36). NDM types contributed to 35% (30/85) of all types found in Victoria, 67% (8/12) of all types found in South Australia and 39% (7/18) of all types found in Western Australia.

Ribosomal methyltransferases were often detected among isolates containing NDM types (29%, 19/65; *rmtB* [14], *armA* [3], *rmtB* + *rmtF* [1] and *rmtB* + *rmtE* [1]).

KPC types were mostly reported from Victoria (53%; 10/19), although reports were noted in three other states (New South Wales, *n* = 4; South Australia, *n* = 4; and Queensland, *n* = 1).

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

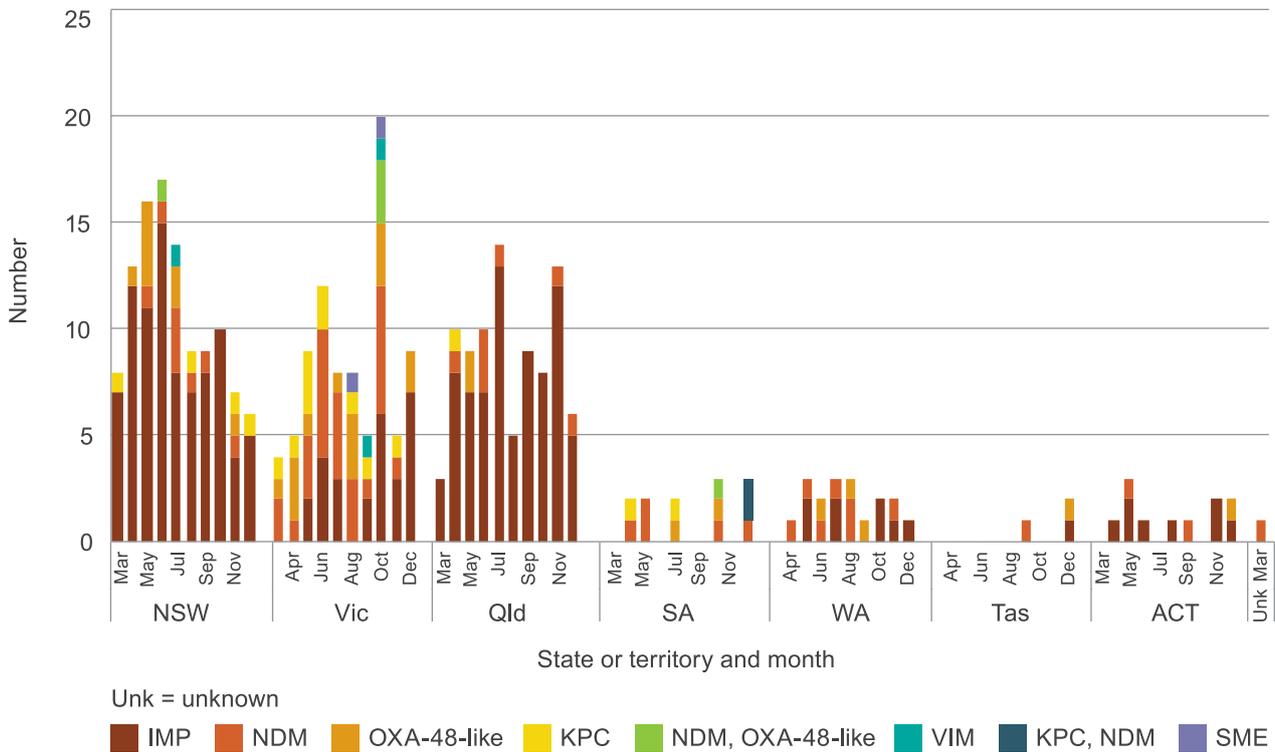
The distribution of carbapenemase types by state and territory, and month of confirmation is shown in Figure 5.9. The sharp increase in October 2016 for Victoria reflects several isolates that were collected in September 2016. Of interest is the emergence of two *Serratia marcescens* isolates with SME type in Victoria. Increasing numbers of SME carbapenemases are being reported around the world, especially in the Americas.

Carbapenemase-producing Enterobacteriaceae by organism

Carbapenemases were found in 16 species of Enterobacteriaceae. IMP-type carbapenemase accounted for 64% (208/326) of all carbapenemases, and was found in 13 different species (Figure 5.10). *E. cloacae* complex accounted for 46% (96/208) of all IMP-type carbapenemases and 29% (96/326) of all CPE. However, in Queensland, 55% (48/87) of all CPE reported were *E. cloacae* complex containing IMP types. NDM and OXA-48-like carbapenemase types were found mainly in *Escherichia coli* (60%, 39/65 for NDM; 64%, 23/36 for OXA-48); however, when both NDM and OXA-48-like or KPC types were found together, they were mainly in *K. pneumoniae* (86%; 6/7). One KPC (5%; 1/19) was found in *Citrobacter farmeri*.

Carbapenemases were found in 16 species of Enterobacteriaceae.

Figure 5.9: Carbapenemase types reported, by month, and state and territory, 17 March – 31 December 2016



Source: CARAlert

Other critical antimicrobial resistance types

Ceftriaxone-nonsusceptible *N. gonorrhoeae* was reported from New South Wales, and contributed to 17% (4/24) of all *N. gonorrhoeae* submitted to CARAlert in July 2016.

For *S. aureus*, 98% were daptomycin-nonsusceptible strains (62/63). One vancomycin-nonsusceptible (vancomycin-intermediate) strain was confirmed in June 2016 from Victoria. No linezolid-nonsusceptible *S. aureus* strains were reported.

Ribosomal methyltransferases were detected in 37 isolates of Enterobacteriaceae, representing seven species; 57% (21/37) of these also had a carbapenemase. Five ribosomal methyltransferase genes were found: *rmtB* (59%; 22/37), either alone (20; 54%) or in combination with *rmtE* (1; 2.5%) or *rmtF* (1, 2.5%); *armA* (27%; 10/37); *rmtC* (8%; 3/37);

and *rmtF* alone (1; 3%). Two isolates had multiple genes: *Providencia rettgeri* (*rmtB*, *rmtE* and NDM) and *K. pneumoniae* (*rmtB*, *rmtF* and NDM + OXA-48-like).

No *Streptococcus pyogenes* with penicillin reduced susceptibility was detected in this period.

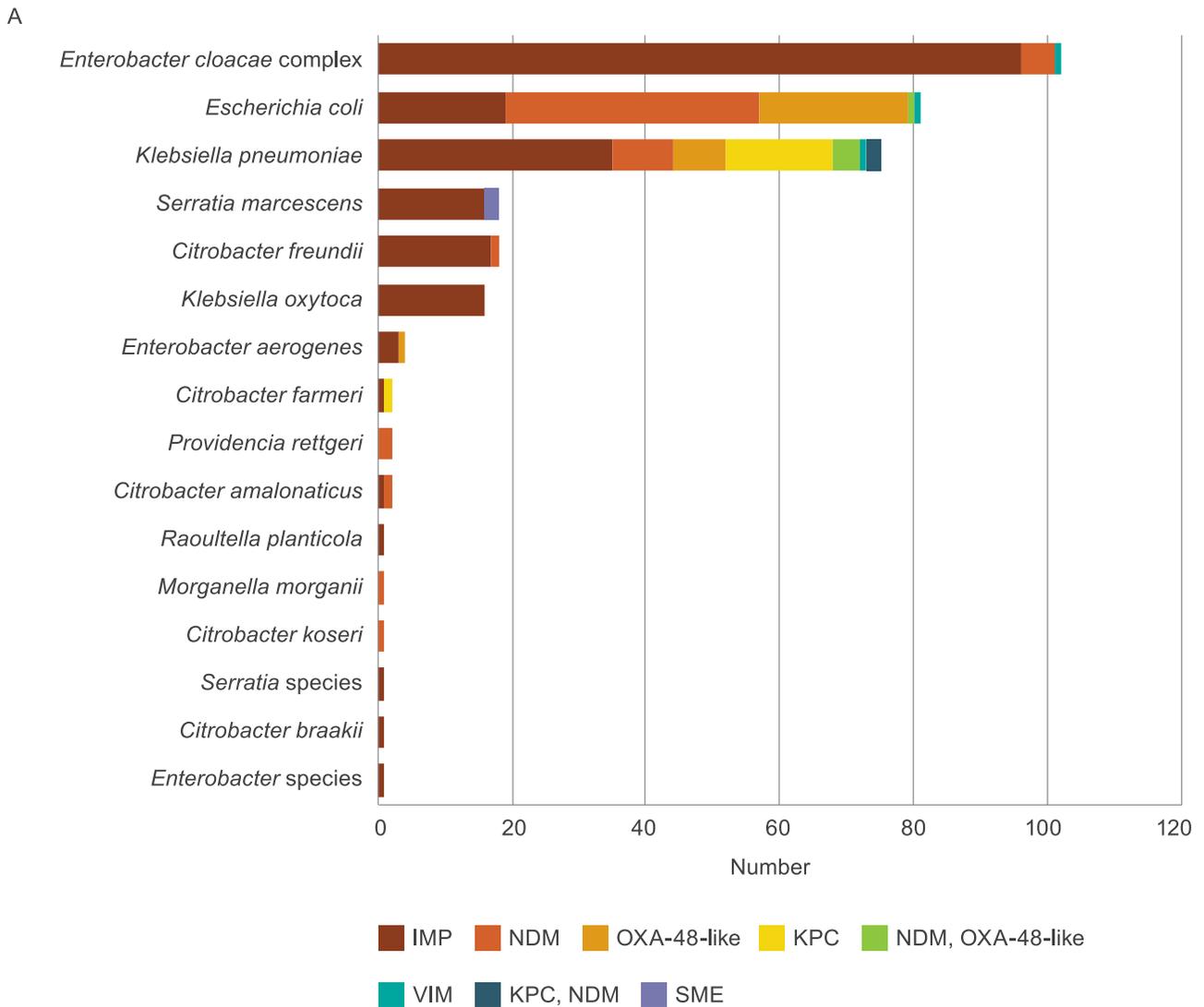
5.3 Conclusion

CARAlert was established in 2016, and has successfully operated with the collaboration and support of the states and territories, and originating and confirming laboratories across the country. All states and territories submitted at least one CAR, and 70 originating laboratories contributed CARs.

The Commission will continue to monitor records from CARAlert and prepare regular summary reports; the volume of CARs will inform the frequency of these reports. The reports are used by health departments to inform working parties



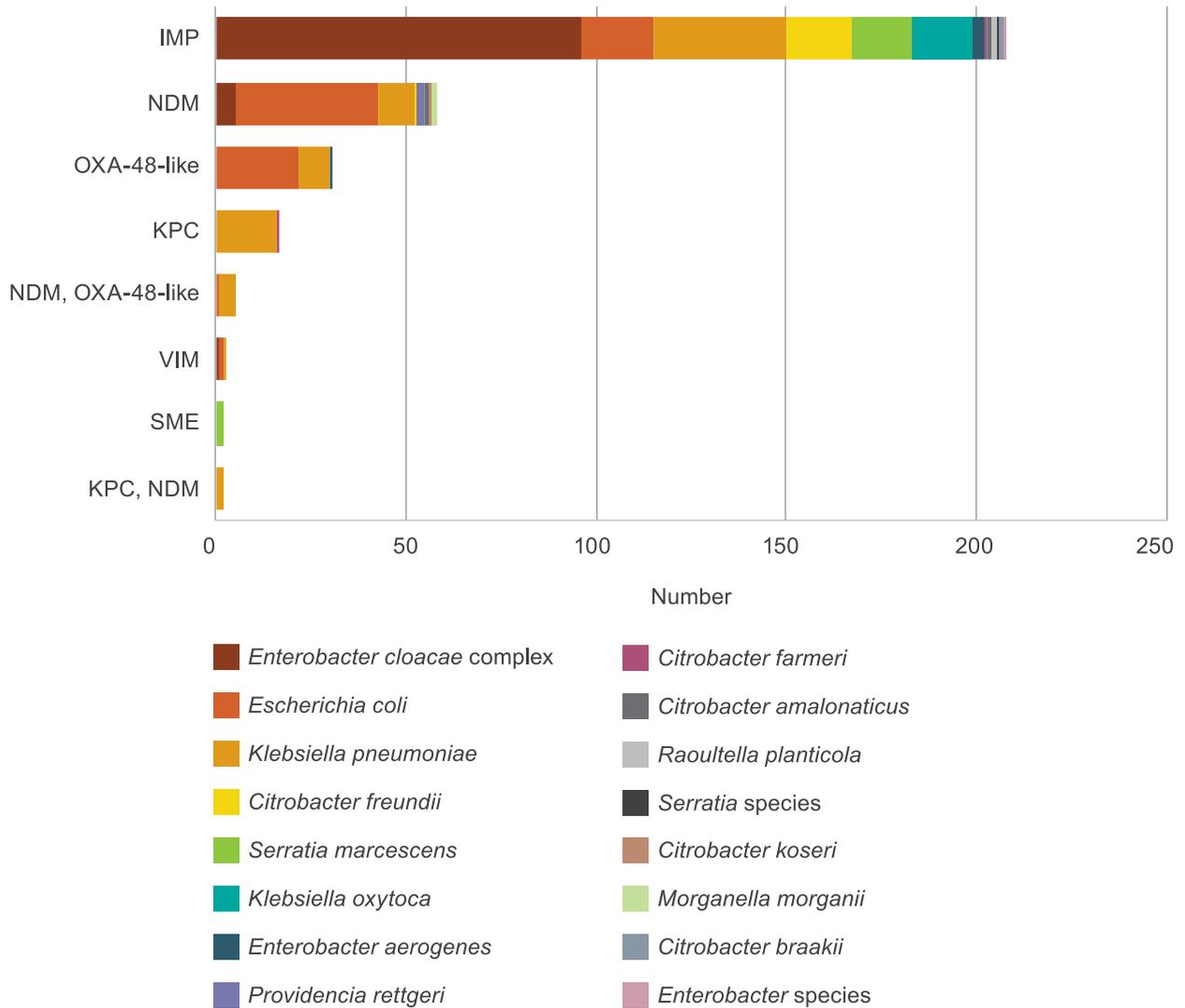
Figure 5.10: Carbapenemase-producing Enterobacteriaceae reported by A) species and carbapenemase type and B) carbapenemase type by species, 17 March – 31 December 2016



continued

Figure 5.10: continued

B



Source: CARAlert

for microbiology and communicable diseases networks that monitor results for any evidence of outbreaks, particularly of CPE. The Commission will provide additional reports to the states and territories, as required; however, authorised state and territory officers now have direct access to CARAlert, which reduces the need for ad hoc reports.

CARAlert summary reports are used by health departments to inform working parties for microbiology and communicable diseases networks that monitor results for any evidence of outbreaks, particularly of CPE.

The number of records in the database to date means that it is not yet possible to draw specific conclusions from the analyses. However, the data undergo regular epidemiological analysis, and, as the data collection develops and the numbers of reports increase to enable meaningful analyses of trends and their implications, these aspects will also be reported on. It is anticipated that the data will inform quality improvement initiatives and policies to reduce antimicrobial resistance.

A CARAlert handbook was produced to assist participants during the establishment phase and promote a coordinated approach to data collection. The handbook is currently under review, for reissue by June 2017. During the review, all CARs will be examined for their suitability to remain on the list, and additional CARs will be considered for inclusion.

Area for action

Implement actions to control carbapenemase-producing Enterobacteriaceae

Data from the National Alert System for Critical Antimicrobial Resistances (CARAlert) show that carbapenemase-producing Enterobacteriaceae were the most frequently recorded critical antimicrobial resistance between March and December 2016. The IMP-type carbapenemase is now endemic on the Australian eastern seaboard.

The Australian Commission on Safety and Quality in Health Care has published *Recommendations for the Control of Carbapenemase-producing Enterobacteriaceae (CPE): A guide for acute care health facilities* and will work with health service organisations to support timely implementation of these recommendations.

Area for action

Monitor resistant gonococcal infections to inform treatment guidelines

The National Alert System for Critical Antimicrobial Resistances (CARAlert) reports on isolates of *Neisseria gonorrhoeae* that are non-susceptible to ceftriaxone or azithromycin. Strains that are non-susceptible to azithromycin are more common than initially thought. CARAlert data complement state and territory systems that monitor antimicrobial resistance as part of prevention and control strategies for sexually transmissible infections. The emergence of antimicrobial-resistant *N. gonorrhoeae* at the same time as continued increases in disease notifications may lead to treatment failures and disease transmission.

Treatment guidelines for gonococcal infection should be reviewed in light of emerging non-susceptibility to azithromycin. The Australian Commission on Safety and Quality in Health Care will work with the states and territories to provide regular updates on ceftriaxone- or azithromycin-nonsusceptible *N. gonorrhoeae* through CARAlert, as well as to inform national and local treatment guidelines.



Chapter 6

Focus areas

Key messages

- Vancomycin-resistant enterococci (VRE) have emerged as a major healthcare problem in Australia. When enterococci are resistant to vancomycin, only two or three reserved antimicrobials can be used to treat serious infections.
- The Queensland clone of methicillin-resistant *Staphylococcus aureus* (MRSA) has become the dominant community-associated MRSA (CA-MRSA) clone in Australia. CA-MRSA is now a more common cause of bloodstream infection than healthcare-associated MRSA. In *S. aureus*, resistance to methicillin is the hallmark of acquired resistance to almost all β -lactams. Community-onset infections caused by strains of MRSA are therefore likely to fail treatment with the usual β -lactams used by community practitioners, resulting in hospitalisation for treatment with parenteral antimicrobials.
- Rates of resistance in Australia compared with other countries have changed little between 2014 and 2015. Antimicrobial dispensing rates in the Australian community are substantially higher than in benchmark countries.
- Three susceptibility testing systems are currently used in laboratories in Australia: Clinical and Laboratory Standards Institute, European Committee on Antimicrobial Susceptibility Testing, and Calibrated Dichotomous Sensitivity (developed in Australia). The Antimicrobial Use and Resistance in Australia Surveillance System analyses and reports on data longitudinally, and use of different testing systems can make it difficult to compare resistance rates. A nationally standardised approach would simplify data collection and analysis, assist in benchmarking and increase confidence in long-term trends.



This chapter explores some key issues for antimicrobial use (AU) and antimicrobial resistance (AMR) that highlight the importance of surveillance and the responses that may be required. It also includes comparisons of Australia's AU and AMR with other countries.

6.1 The growing problem of vancomycin-resistant enterococci

Enterococci are opportunistic pathogens that cause a range of infections in patients whose physical barriers are compromised through surgery or invasive devices. They rarely cause disease in healthy people, but may cause infections in vulnerable patients, such as very elderly people or those who are immunosuppressed (see Chapter 4). The two most medically important species are *Enterococcus faecalis* and *E. faecium*.

Comparatively few antimicrobial agents are active against enterococci. Clinicians rely on vancomycin to treat serious penicillin-resistant infections acquired in hospital caused by *E. faecium*. However, vancomycin-resistant enterococci (VRE) have emerged as a major healthcare problem in Australia. When enterococci are resistant to vancomycin, only two or three reserved antimicrobials can be used to treat serious infections.

Vancomycin resistance in *Enterococcus* species can be intrinsic, as occurs in some uncommon species (such as *E. gallinarum* and *E. casseliflavus*), but acquired resistance caused by highly mobile transposons and plasmids is the cause of the recent rapid increase in VRE infections in Australian hospitals. Eight types of gene complexes have so far been described⁵⁰, but only two are common: *vanA* and *vanB*. The VanA phenotype of resistance (encoded by the *vanA* gene complex) has been the main type of VRE observed in most countries. In Australia, the

dominant phenotype has historically been VanB, although this situation is changing.

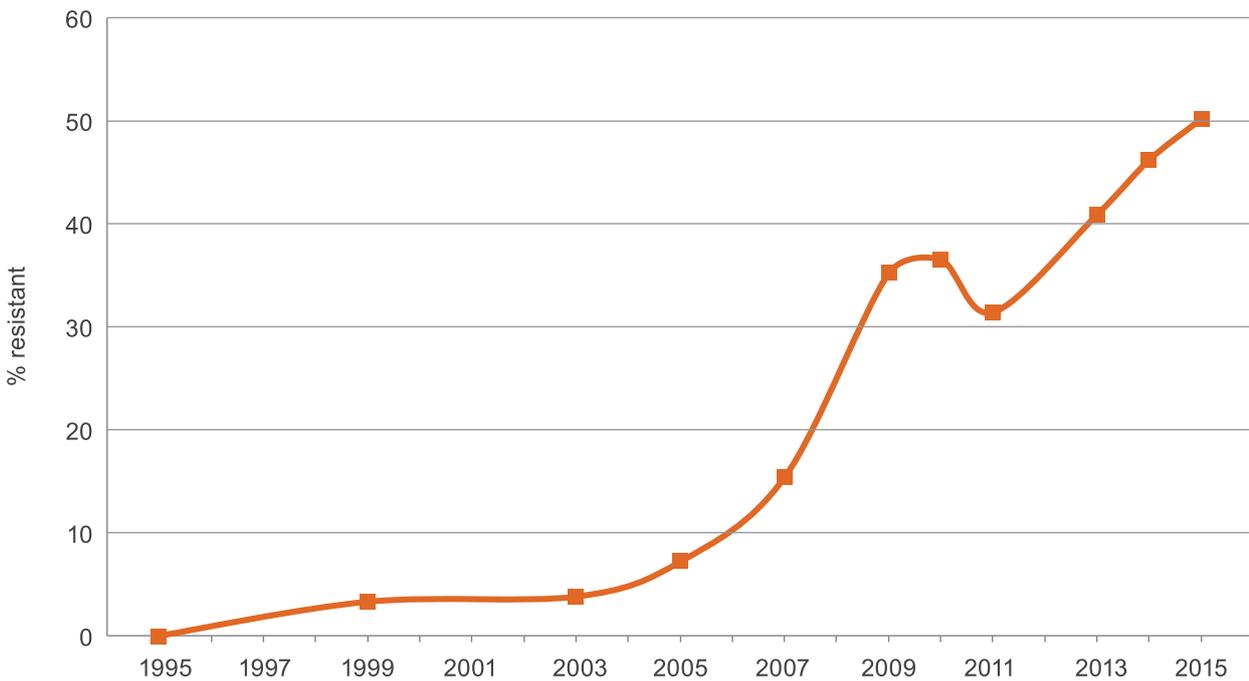
VRE were first isolated in England and France in 1988.⁵¹ They were subsequently reported in the United States in 1989, where their prevalence increased rapidly over the next five years.⁵⁰ The first reported infection with VRE in Australia occurred in 1994.⁵²

The Australian Group on Antimicrobial Resistance (AGAR) has been conducting intermittent surveys of enterococci causing infection since 1995. At that time, VRE were rare in Australia, and none were detected in the first survey conducted in 1995.

The clinical picture of VRE infections is similar worldwide – the less common of the two medically important species, *E. faecium*, is the dominant cause of infections with VRE.⁵³ This may be a consequence of the broader range of antimicrobials to which this species is resistant. In particular, ampicillin resistance has become very common in hospital-adapted *E. faecium*.

AGAR has surveyed VRE in 1995, 1999, 2003, 2005, 2007, 2009, 2010, 2011, and each year since 2013.⁵⁴⁻⁶¹ From 2011 onwards, surveys have been based on blood culture isolates collected continuously throughout the year. Figure 6.1 shows the percentage of *E. faecium* isolates that were resistant to vancomycin from 1995 to 2015. The proportion of resistant isolates in Australia increased rapidly from 2005, and is now higher than that in any European country (see Section 6.3).

The emergence and spread of vancomycin-resistant *E. faecium* have occurred unevenly across the country. The AGAR surveys show that it first emerged and spread rapidly in Victoria, then in New South Wales and then in South Australia. Some years later, it appeared in Queensland, the Australian Capital Territory and the Northern Territory. Rates are much lower in Western Australia than in other states and territories.

Figure 6.1: Vancomycin resistance in *Enterococcus faecium* in Australia, 1995–2015

Notes:

1. Vancomycin resistance is defined as a minimum inhibitory concentration >4 mg/L.
2. The sampling method and the number of contributing laboratories changed after 2010, which accounts for the initial dip in 2011.

Source: AGAR surveys

Until recently, Australian VRE have been very strongly dominated by the VanB phenotype. The VanA phenotype was first detected in a single isolate (1.3%) in the 2009 AGAR survey; in the same year, 77 isolates were of the VanB phenotype. Since then, the VanA phenotype has made up an increasing proportion of VRE, reaching 36.2% in *E. faecium* in 2015.⁶¹ This is important because there are even fewer therapeutic options for VanA-type resistance than for the VanB type. A recent study of AGAR data suggested that there is reduced 30-day survival in patients with VanA-type *E. faecium* bloodstream infection compared with VanB type.⁶²

The increasing proportion of the VanA phenotype is significant because there are even fewer therapeutic options for VanA-type resistance than for the VanB type.

In contrast to the situation with *E. faecium*, vancomycin resistance in *E. faecalis* has remained uncommon in Australia: the rate was 0.2% (3/1,987) in 2005, and 0.9% (5/560) in 2015.

The reasons for the rapid rise of VRE in Australia have not been fully elucidated. Contributing factors include the following:

- Almost all VRE are *E. faecium*, the species that is strongly associated with infections related to hospital care⁶¹ and has acquired resistance to a wider range of antimicrobials (particularly penicillin) than *E. faecalis*
- High antimicrobial exposure in patients who are most at risk (such as those on renal dialysis or liver transplant recipients) promotes colonisation with VRE or amplifies VRE in patients who are already colonised
- The *vanB* gene complex has been found in the anaerobic normal gut flora of healthy people⁶³, which acts as a reservoir for vancomycin resistance that can be transmitted to vancomycin-susceptible enterococci⁶⁴

Community-acquired methicillin-resistant Staphylococcus aureus clones now play a substantial role in hospital-onset S. aureus infections. This is not surprising because a significant proportion of healthcare-associated staphylococcal infections are caused by strains that the patient already carries, but cause infection after the healthcare intervention.

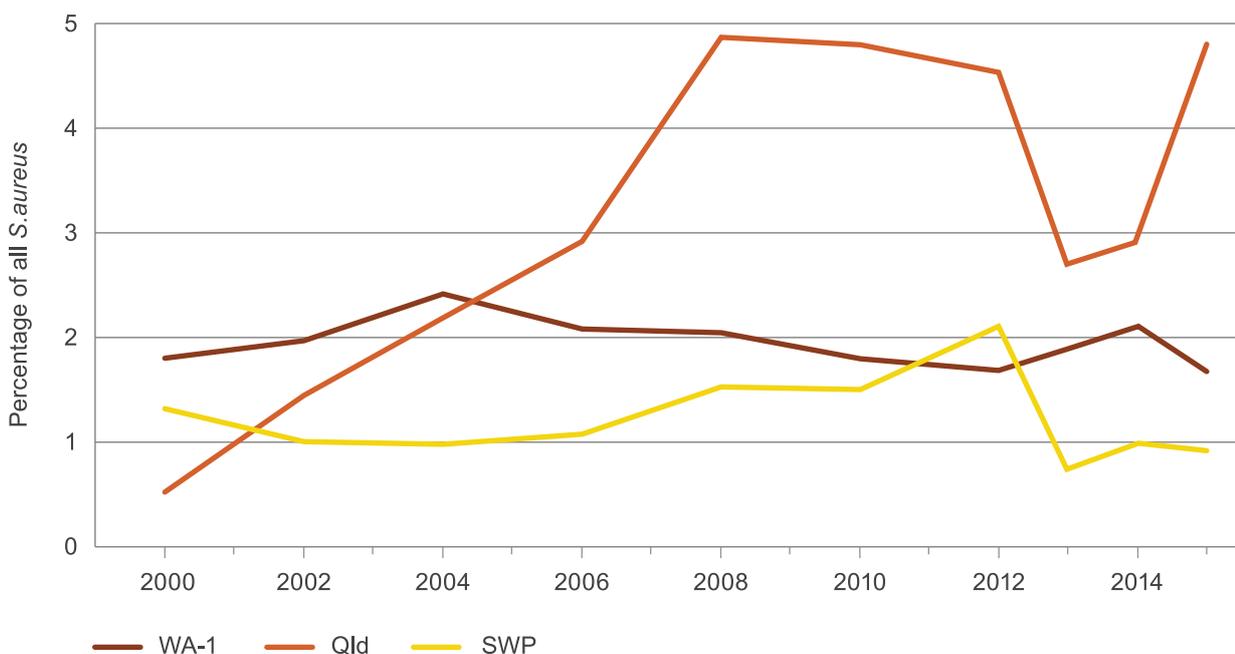
The Queensland clone has become the dominant clone of CA-MRSA in Australia. It was first detected in southern Queensland in 2000⁶⁸, considerably later than the other prominent CA-MRSA clones, WA-1 and SWP. It has since spread to become the dominant CA-MRSA clone in Queensland, the Northern Territory, South Australia, Victoria and Western Australia, and occurs at an equal rate to WA-1 in New South Wales.⁶⁹ It tends to be susceptible to

non- β -lactam classes of antimicrobials, and also usually produces PVL. The reasons for its rapid spread and dominance remain unclear, despite extensive molecular studies; it harbours very few virulence factors other than PVL.⁷⁰

Overseas studies have noted that strains that produce PVL have a lower propensity to cause invasive infection.^{71,72} In 2015, 82% of Queensland CA-MRSA was PVL-positive.

Trends in CA-MRSA, including the Queensland clone, as a percentage of all *S. aureus* from AGAR surveys are shown in Figure 6.2. From 2013 onwards, AGAR surveys have focused on bloodstream infections and continuous collection of episode data. The drop in percentage observed in 2013 relates to the switch to surveying only bloodstream isolates, but – since 2013 – the trend in the proportion of Queensland CA-MRSA has been increasing. The Queensland CA-MRSA clone first became dominant in 2006, only six years after it was first detected. In 2015, Queensland CA-MRSA accounted for 31% (89/283) of all CA-MRSA across Australia.⁶⁹

Figure 6.2: Trends in the three main clones of CA-MRSA in Australia, 2000–2015



CA-MRSA = community-associated methicillin-resistant *Staphylococcus aureus*

Source: AGAR surveys

Figure 6.3 shows the trends in Queensland CA-MRSA across the states and territories. The clone is particularly prominent in the Northern Territory, where it accounted for 20% of all bloodstream isolates in 2015.⁶⁹ The decrease in proportions in 2013 in Victoria, Queensland and Western Australia related to the switch to bloodstream surveillance. Since then, proportions have begun to increase again in those three states.

CA-MRSA has become a major problem in Australia, and is now a more common cause of bloodstream infection than HA-MRSA. This means that more patients will be treated with vancomycin and related agents, generating increasing selection pressure for other multidrug-resistant pathogens such as VRE. A further challenge for health care is that, so far, no country has found effective interventions to control the spread of CA-MRSA. Effort in this area is a priority.

6.3 International comparisons

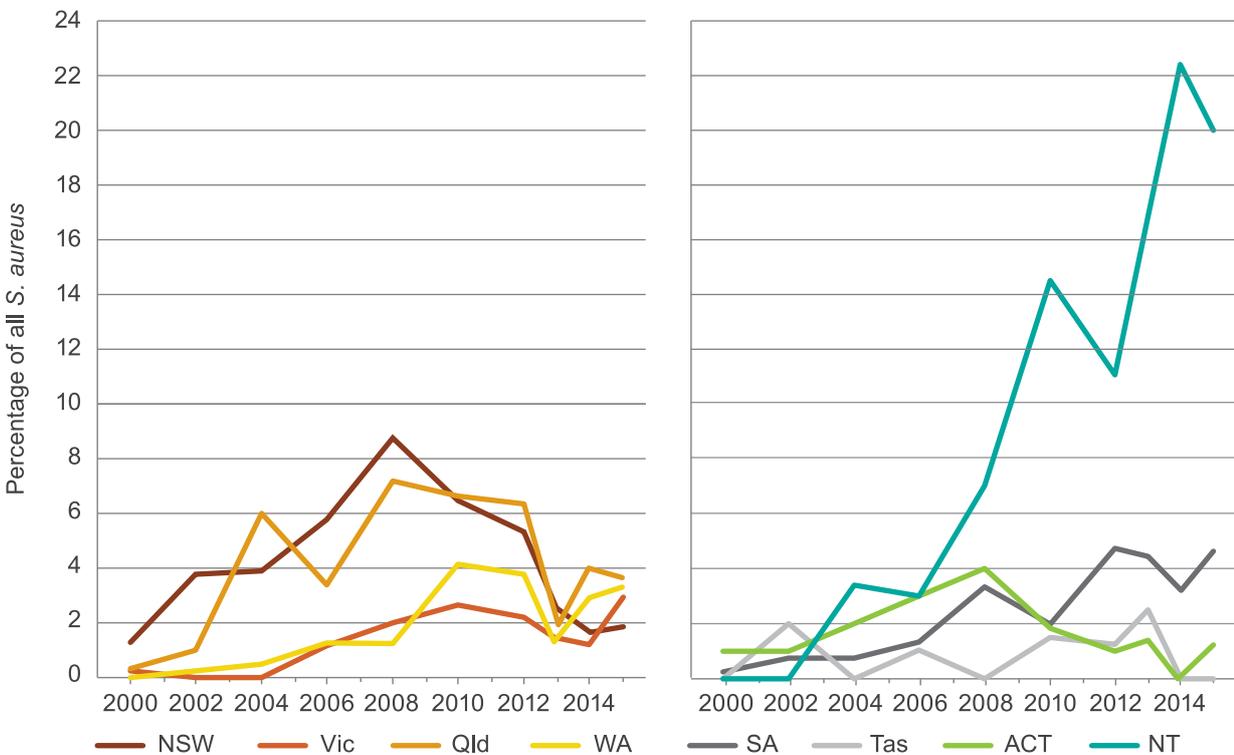
A detailed comparison of AU and AMR between Australia and other countries was provided in the 2016 report of the Antimicrobial Use and Resistance in Australia (AURA) project, mainly using data from 2014. A review of 2015 data revealed few changes of note.

Antimicrobial use in the community

Comparable data for AU in the community are available from European countries through the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) for 2015⁷³, and for Canada from 2014.⁷⁴

Rates of resistance in Australia compared with other countries have changed little between 2014 and 2015.

Figure 6.3: Trends in Queensland CA-MRSA across states and territories, 2000–2015



CA-MRSA = community-associated methicillin-resistant *Staphylococcus aureus*
 Source: AGAR surveys

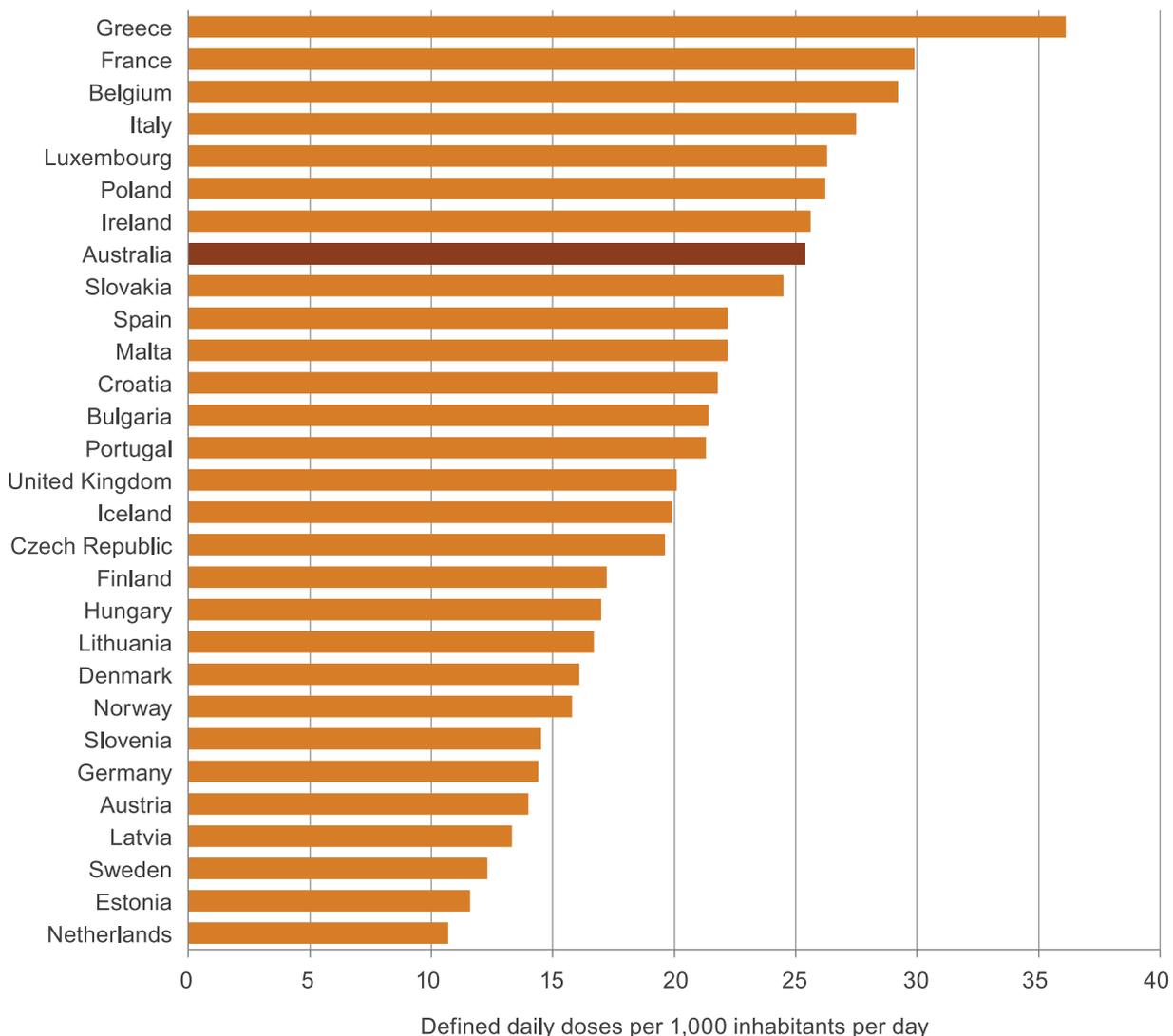
Figure 6.4 demonstrates comparisons with European countries by defined daily doses (DDDs) per 1,000 inhabitants per day. Australia ranked between the seventh and eighth highest of 28 European countries in 2015, compared with between the fifth and sixth highest in 2014, even though AU measured as DDDs per 1,000 inhabitants per day increased in Australia in 2015.

Figures 6.5 and 6.6 compare Australia with benchmark countries by DDDs per 1,000 inhabitants per day, and prescriptions filled per 1,000 inhabitants per year. When compared

with benchmark countries, antimicrobial dispensing rates in Australia are substantially higher than in Sweden⁴⁰, Denmark⁴¹, Norway⁴², the Netherlands⁷⁵, England⁷⁶, Scotland⁷⁷ and Canada.⁷⁴ This ranking has not changed since 2014.

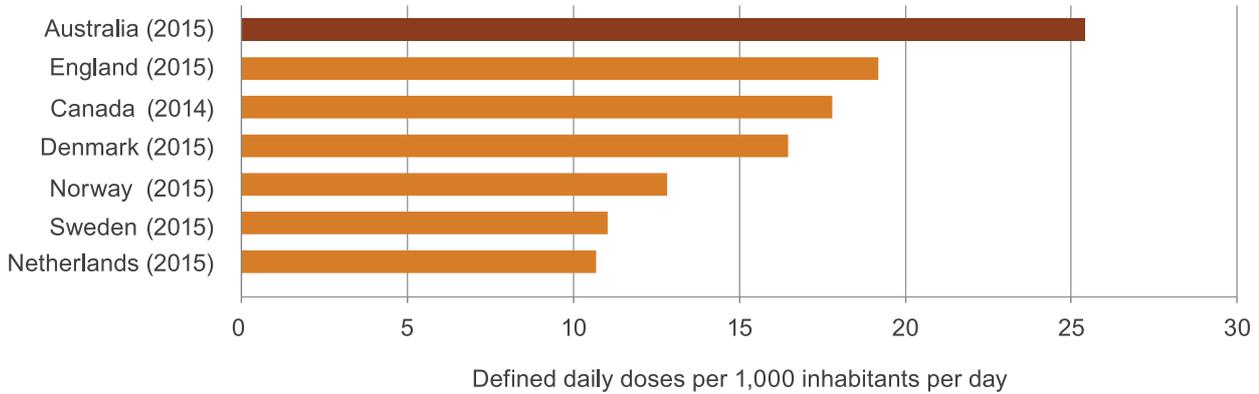
Antimicrobial dispensing rates in the Australian community are substantially higher than in benchmark countries.

Figure 6.4: Comparison of community antimicrobial use in Australia and 28 European countries, 2015



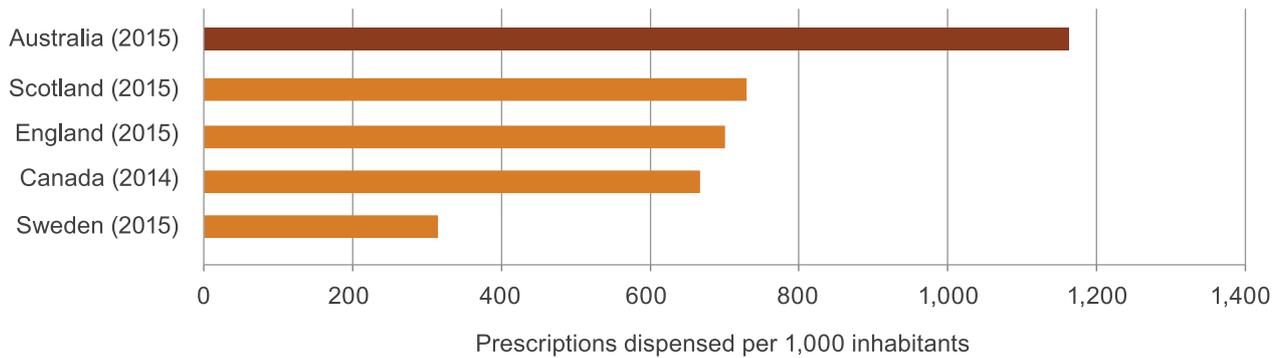
Sources: ESAC-Net (Europe)⁷³; PBS (Australia)

Figure 6.5: Comparison of community antimicrobial use in Australia and other similar countries, DDD/1,000 inhabitants per day



Sources: PBS (Australia); CIPARS (Canada); DANMAP (Denmark); ESPAUR (England); NethMAP (Netherlands); SWEDRES (Sweden)

Figure 6.6: Comparison of community antimicrobial use in Australia and other similar countries, by number of prescriptions dispensed



Sources: PBS (Australia); CIPARS (Canada); ESPAUR (England); SAPG (Scotland); SWEDRES (Sweden)

Antimicrobial use in hospitals

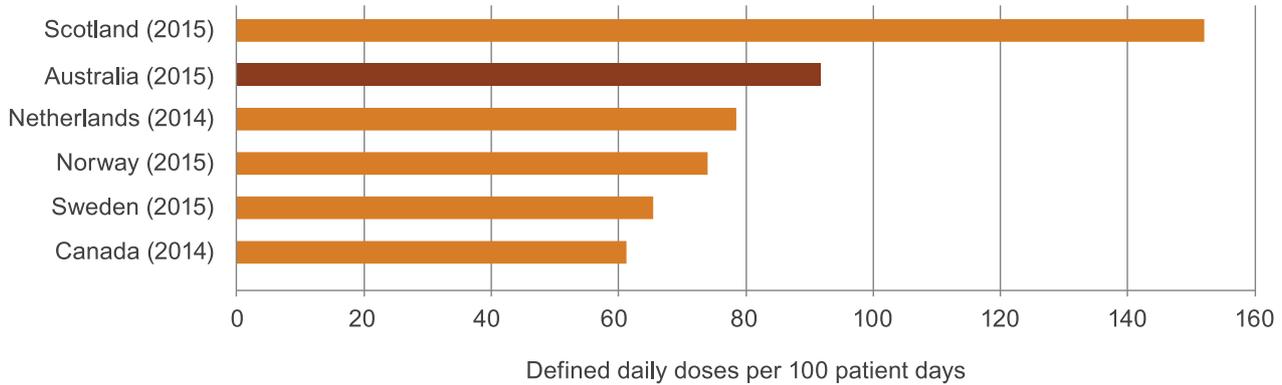
Comparison of the patterns of hospital prescribing in hospitals across a range of benchmark countries shows some important differences from those in the community. Data were available from individual surveillance programs only: from England⁷⁶, Scotland⁷⁷, Sweden⁴⁰, Denmark⁴¹ and Norway⁴² for 2015; and from Canada⁷⁴ and the Netherlands⁷⁵ for 2014. Figure 6.7 compares countries by DDDs per 100 patient days, and Figure 6.8 compares countries by DDDs per 1,000 inhabitants per day. Australia ranked higher than all comparator countries except Scotland.

Commentary on antimicrobial use

Australia has sustained high use of antimicrobials in the community, as shown in Chapter 3. This far exceeds the expected use compared with other countries that have similar systems and levels of health care. The reasons for this comparatively high use remain to be fully explained, but, undoubtedly, the high use of agents for upper respiratory infections – most of which have a viral cause or are self-limiting – is a major contributing factor.

Programs such as those run by NPS MedicineWise have been directed at both the general public and community prescribers, with the aim of reducing unnecessary AU in the community. Efforts need to be broadened and intensified if there is to

Figure 6.7: Comparison of hospital antimicrobial use in Australia and other similar countries, DDD/100 patient days

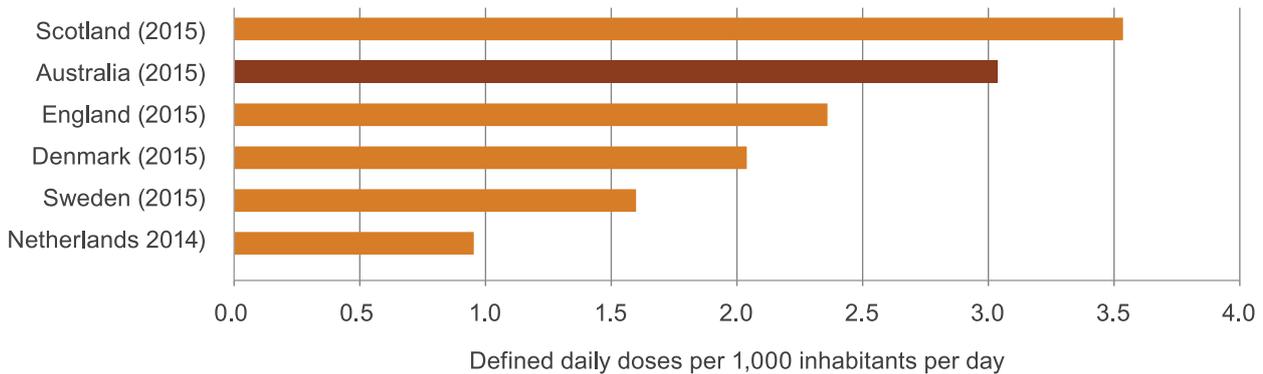


Notes:

1. For the purposes of comparison, patient days and occupied bed days were taken to be equivalent.
2. NAUSP data for Australia were extrapolated to a national estimate by dividing the 2014-15 total number of patient days published by the Australian Institute of Health and Welfare by the total number of occupied bed days recorded by NAUSP contributors.

Sources: NAUSP (Australia); CIPARS (Canada); NethMAP (Netherlands); SAPG (Scotland); NORM (Norway); SWEDRES (Sweden)

Figure 6.8: Comparison of hospital antimicrobial use in Australia and other similar countries, DDD/1,000 inhabitants per day



Notes:

1. For the purposes of comparison, patient days and occupied bed days were taken to be equivalent.
2. NAUSP data for Australia were extrapolated to a national estimate by dividing the 2014-15 total number of patient days published by the Australian Institute of Health and Welfare by the total number of occupied bed days recorded by NAUSP contributors.

Sources: NAUSP (Australia); DANMAP (Denmark); ESPAUR (England); NethMAP (Netherlands); SAPG (Scotland); SWEDRES (Sweden)

be any substantial and sustained reduction in unnecessary community AU.

As described in the 2015 National Antimicrobial Utilisation Surveillance Program (NAUSP) report²⁰ and Chapter 3, AU has steadily decreased in Australian hospitals in the past few years; there was a further 2% reduction between 2014 and 2015. This can be attributed to the steadily increasing number of hospitals that are developing and implementing antimicrobial stewardship (AMS) programs, encouraged

by the hospital accreditation requirements in the Preventing and Controlling Healthcare Associated Infection Standard of the National Safety and Quality Health Service Standards.⁵ Participation in NAUSP and the National Antimicrobial Prescribing Survey (NAPS) provides health services with detailed local data and analyses, benchmarked against peer hospitals. The NAUSP, NAPS and AURA reports can greatly assist in developing and maintaining effective AMS programs. Continued expansion

and intensification of AMS programs are essential if Australia is to reach the same levels of AU as benchmark countries such as Sweden, Canada and the Netherlands.

Antimicrobial resistance

Australia can currently compare resistance rates for selected pathogens only with European countries, because Europe is the only region of the world that regularly releases comparable data. Data from AGAR can be directly compared with data from the European Antimicrobial Resistance Surveillance Network (EARS-Net) program⁷⁸, because both surveillance systems examine resistance in bacterial pathogens found in blood cultures.

Overall, there is very little difference in the comparisons between 2014 and 2015. Rates of resistance to fluoroquinolones in *Escherichia coli* and *Klebsiella pneumoniae* (represented by resistance to ciprofloxacin) remain very low in Australia compared with most European countries (Figures 6.9 and 6.10). Resistance to third-generation cephalosporins in these two species is similarly low by comparison, although not at low as for fluoroquinolones (Figures 6.11 and 6.12).

Rates of resistance to fluoroquinolones and third-generation cephalosporins in Escherichia coli and Klebsiella pneumoniae remain low in Australia compared with most European countries.

In contrast to the comparison for the two enteric gram-negative bacteria shown in Figures 6.9–6.12, the comparison between Australia and European countries for resistance in two key gram-positive pathogens, *S. aureus* and *E. faecium*, is not as favourable. Australia ranks towards the middle in rates of resistance to

methicillin in *S. aureus* (Figure 6.13), and higher than any European country in rates of resistance to vancomycin in *E. faecium* (Figure 6.14).

Compared with European countries, Australia ranks towards the middle in rates of resistance to methicillin in S. aureus, and higher than any European country in rates of resistance to vancomycin in E. faecium.

European surveillance data do not include clonal analyses of MRSA, so the proportions of CA-MRSA and HA-MRSA in a particular country are not known. In Australia, CA-MRSA has a similar prevalence to HA-MRSA.

Commentary on antimicrobial resistance

International comparisons of resistance rates reveal a mixed picture of Australia's ranking. It is believed that restricting access to fluoroquinolones in both the community and hospitals has greatly assisted in keeping rates of resistance to this antimicrobial class low in Australia, ensuring their ongoing value for treating infections caused by strains that are resistant to other antimicrobial classes.

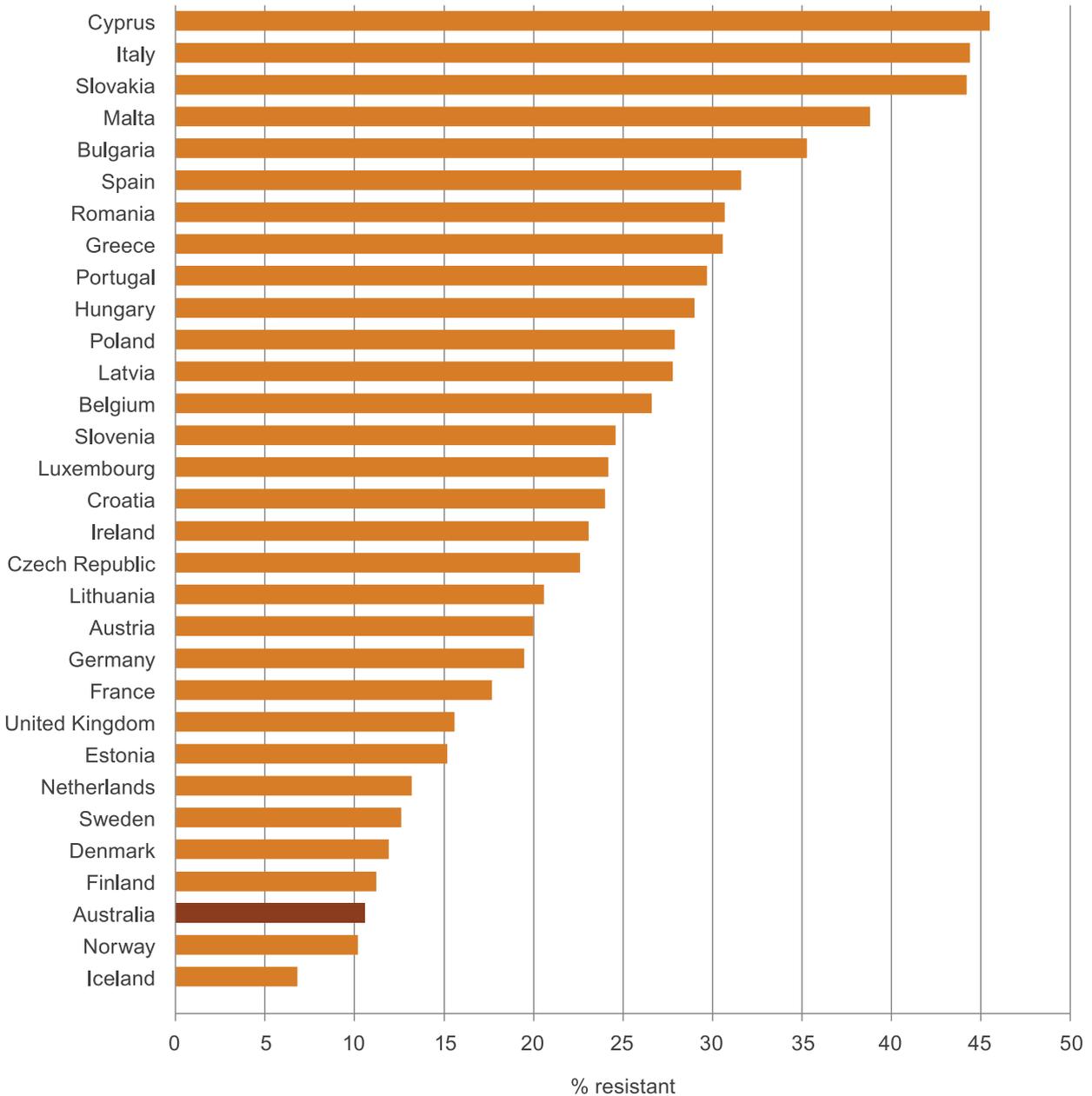
Rates of resistance to third-generation cephalosporins have also remained fairly low in Australia. This antimicrobial class is restricted in the community, but is still widely used in hospitals – often unnecessarily, as shown in the NAPS 2015 report.²²

In contrast, rates of resistance in key gram-positive pathogens are moderate to high in Australia compared with European countries. For MRSA, there has been little change in overall resistance rates in Australia; however, there has been a rapid decline in the prevalence of the multidrug-resistant healthcare-associated

clone, a rise in the United Kingdom–originating EMRSA-15 healthcare-associated clone, and a steady rise in the prevalence of community-associated clones.⁷⁹ The prevalence of

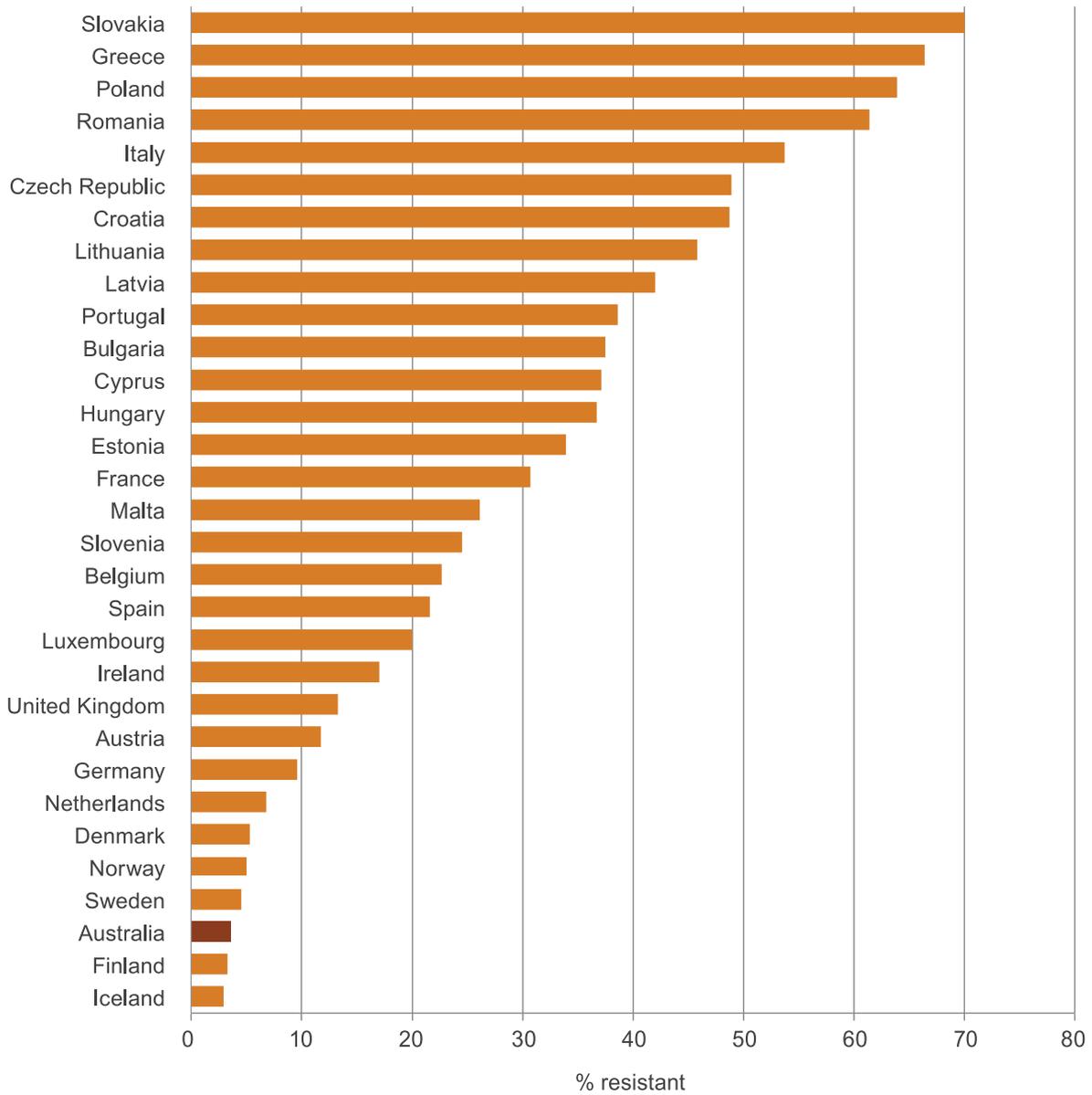
vancomycin resistance in *E. faecium* remains higher in Australia than in any European country; see Section 6.1 for more detail.

Figure 6.9: Comparison of *Escherichia coli* rates of resistance to ciprofloxacin in Australia and European countries, 2015



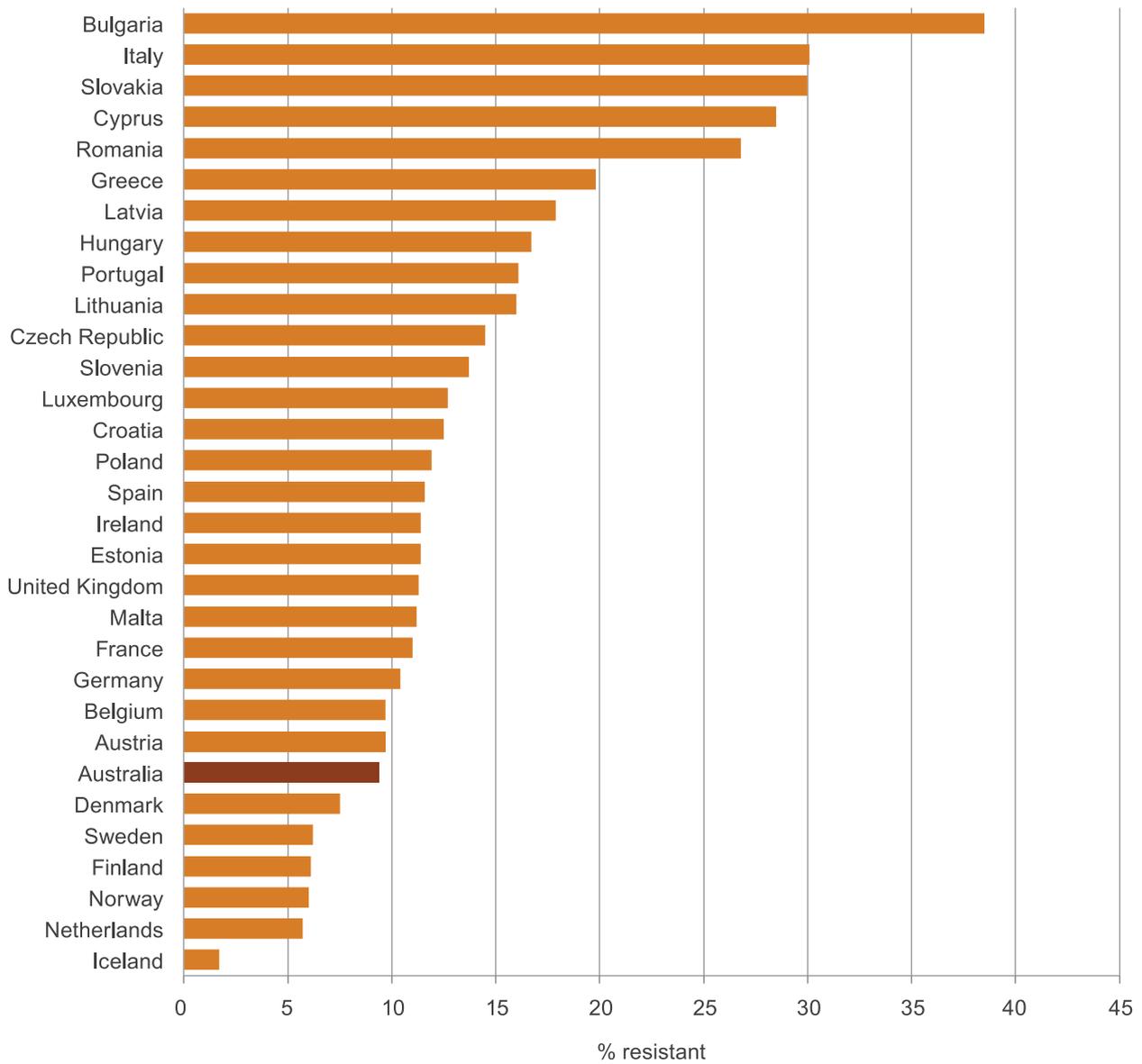
Sources: AGAR (Australia); EARS-Net (Europe)

Figure 6.10: Comparison of *Klebsiella pneumoniae* rates of resistance to ciprofloxacin in Australia and European countries, 2015



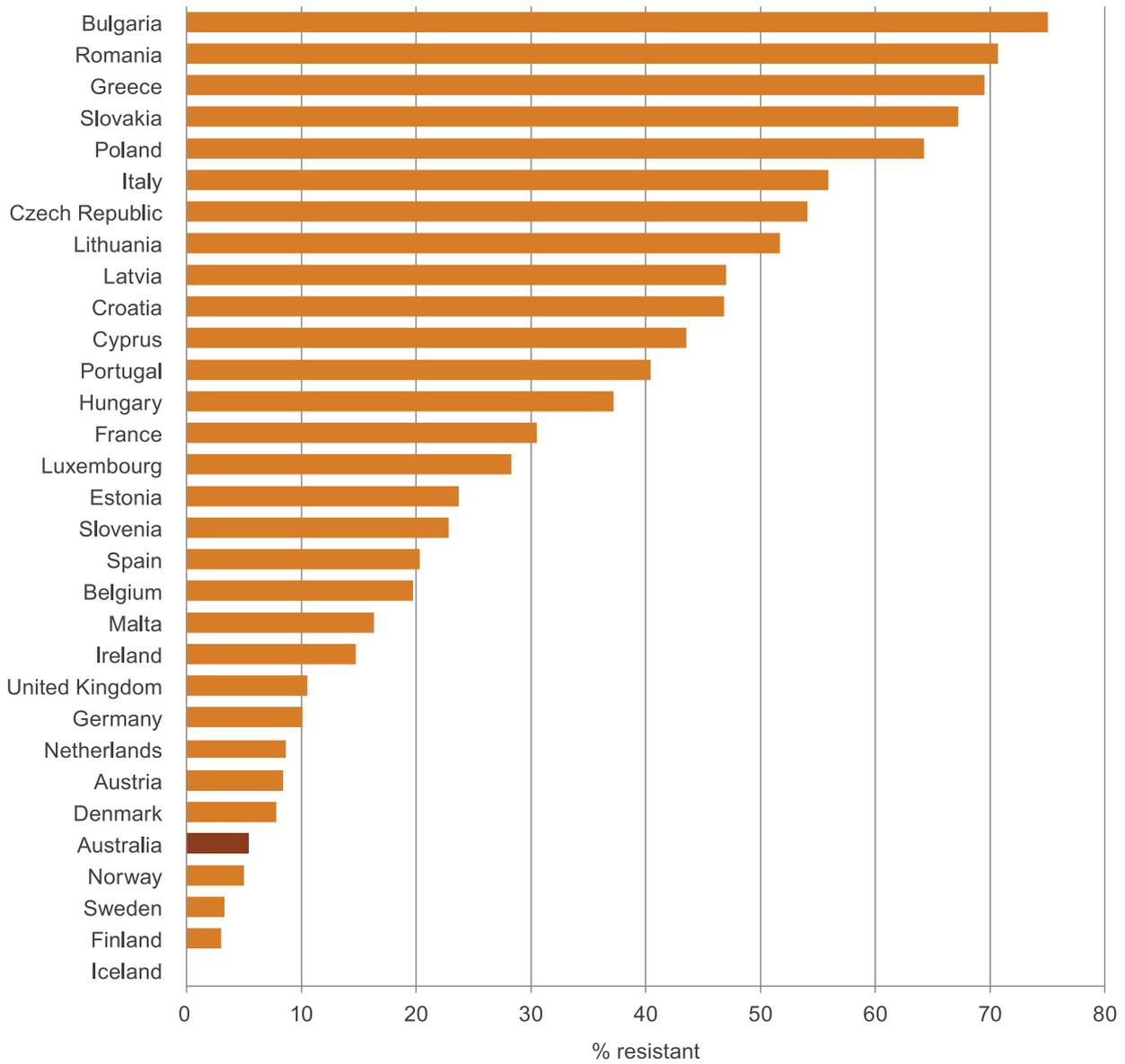
Sources: AGAR (Australia); EARS-Net (Europe)

Figure 6.11: Comparison of *Escherichia coli* rates of resistance to third-generation cephalosporins in Australia and European countries, 2015



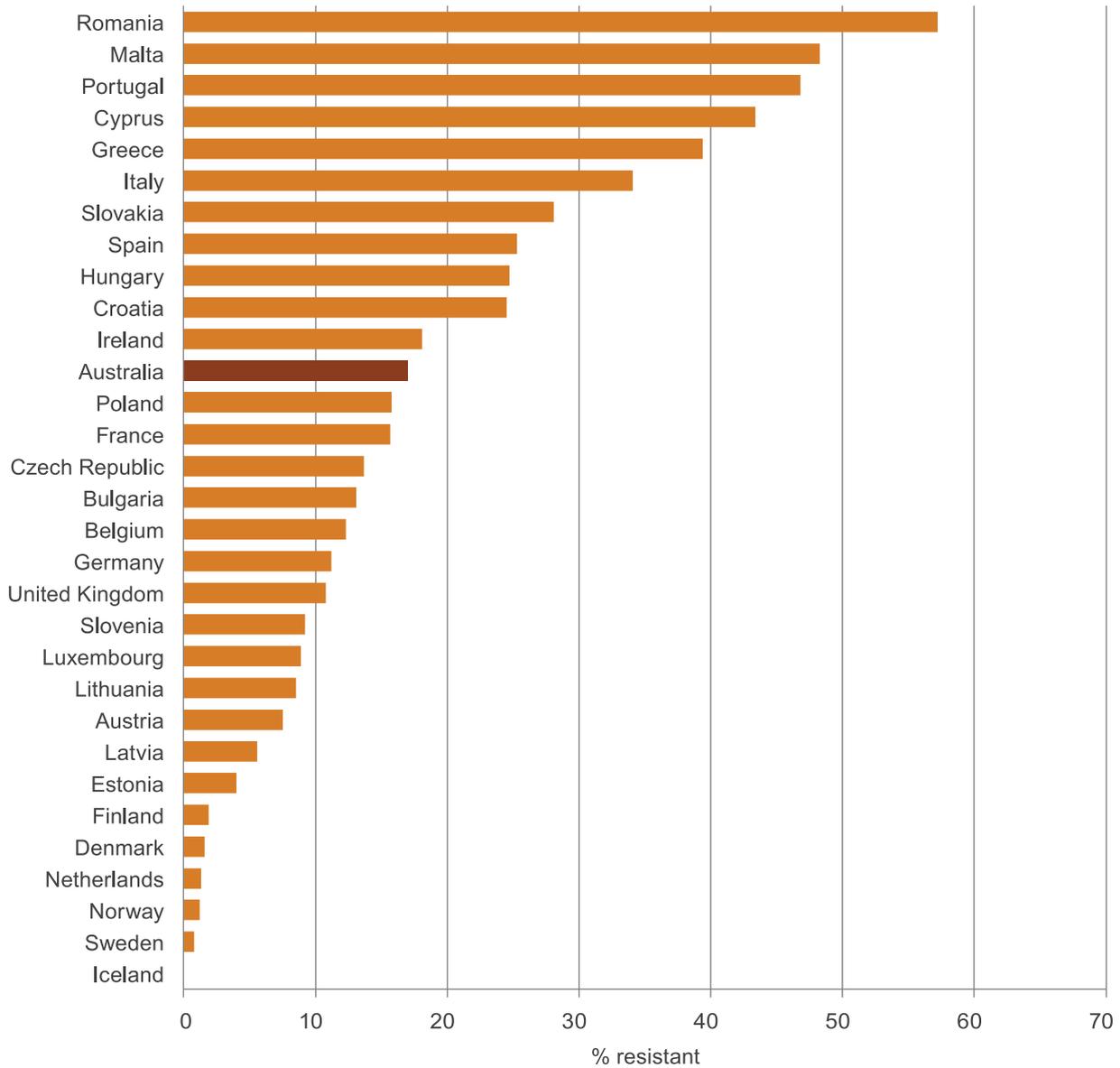
Sources: AGAR (Australia); EARS-Net (Europe)

Figure 6.12: Comparison of *Klebsiella pneumoniae* rates of resistance to third-generation cephalosporins in Australia and European countries, 2015



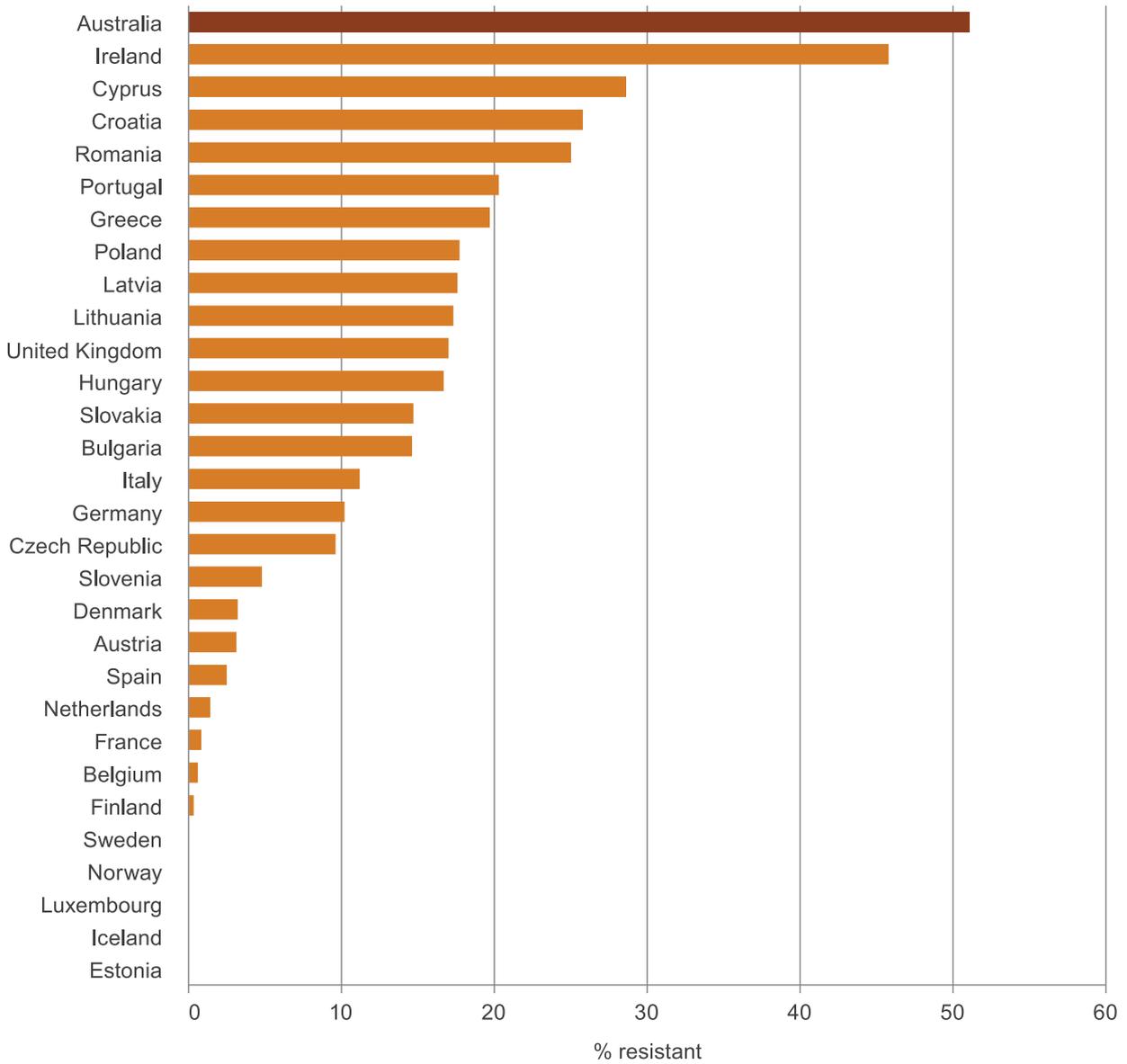
Sources: AGAR (Australia); EARS-Net (Europe)

Figure 6.13: Comparison of *Staphylococcus aureus* rates of resistance to methicillin in Australia and European countries, 2015



Sources: AGAR (Australia); EARS-Net (Europe)

Figure 6.14: Comparison of *Enterococcus faecium* rates of resistance to vancomycin in Australia and European countries, 2015



Sources: AGAR (Australia); EARS-Net (Europe)

6.4 Standardising Australia's approach to susceptibility testing

One of the key elements of the AURA Surveillance System is the national passive surveillance of AMR using data from public and private laboratory systems across Australia. The Australian Commission on Safety and Quality in Health Care (the Commission) has worked with the Queensland Department of Health to use the OrgTRx system as the base IT infrastructure to expand passive AMR surveillance at a national level. Although the AURA coordinating unit acts as the system manager for the national system and coordinates the reporting of these data, it does not own the data and does not control the methods of testing used to generate the data.

For a wide range of diagnostic and laboratory testing, results are reported numerically, usually with reference ranges that have been developed in light of the test and the population the laboratory serves. However, antimicrobial susceptibility testing results are reported categorically – usually as ‘susceptible’, ‘resistant’ and, in some methods, ‘intermediate’. Criteria for interpreting these categories are defined for each testing system and are referred to as ‘breakpoints’.

Breakpoints are set by expert reference groups, considering antimicrobial pharmacology and clinical outcome data for combinations of bacteria and antimicrobials. However, breakpoints differ for each method of susceptibility testing.

The three susceptibility testing systems currently in use in laboratories in Australia are:

- The Clinical and Laboratory Standards Institute (CLSI; based in the United States) system⁸⁰
- The European Committee on Antimicrobial Susceptibility Testing (EUCAST) system⁸¹
- The Calibrated Dichotomous Sensitivity system, which was developed in Australia at the South Eastern Area Laboratory Services.⁸²

Although the systems give broadly similar results and there are some data on differences in laboratory results between CLSI and EUCAST⁸³⁻⁸⁵, no studies have been published that analyse the effect on patient outcomes or AMS.

From the perspective of establishing a surveillance system such as AURA that will analyse and report on data longitudinally, use of different testing methods can make it difficult to compare resistance rates. Although a change in the susceptibility testing system used in a laboratory may affect long-term trend data in a single facility, the ability to determine resistance at the network, state and territory, and national levels is very valuable to policy and program development, and to inform response strategies.

Use of different methods of testing can make it difficult to compare antimicrobial resistance rates, so a standardised approach to testing across Australia is desirable.

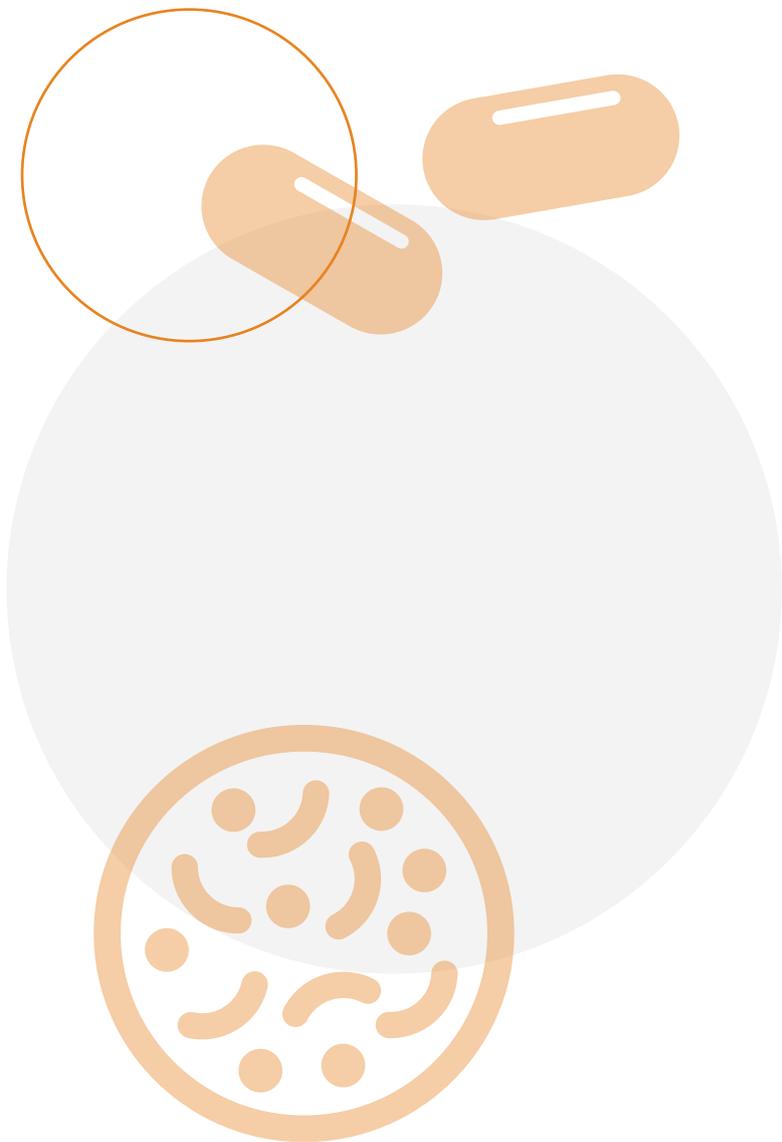
Standardising the approach to testing at a national level has several benefits:

- Discrepancies between results (including percentages of resistant isolates) created by different standard methods for testing, interpretation and breakpoints would be overcome, and there would be
 - greater alignment of view about what the ‘correct’ result is
 - higher concordance between laboratories (within the limits of the system)
 - greater reduction in unwarranted variation in clinical care
 - improved ability for benchmarking between laboratories

- Patient safety would be improved by greater standardisation between diagnostic laboratories – for example, when a patient is admitted to hospital from the community, analyses between hospital- and community-based laboratories would have greater comparability, which would reduce diagnostic uncertainty
- Greater concordance between results from different laboratories would simplify the preparation of antibiograms for AMS programs, and facilitate development of clinical practice guidelines
- National surveillance of AMR would be strengthened by reducing issues around data analysis and reporting
- The ability to contribute effectively to global surveillance proposed by the World Health Organization would be improved.

A nationally standardised approach to antimicrobial susceptibility testing would have several benefits for AURA. It would simplify the collection and analysis of surveillance data, leading to comparable data quality and interpretation. This would assist in benchmarking between sites, and give users more confidence in long-term trends in their local facility's data. This would have flow-on benefits of increasing the utility of the AURA Surveillance System for clinicians.

To encourage the adoption of a national susceptibility testing standard, the Commission has convened a roundtable with stakeholders from laboratories and peak bodies across Australia to discuss this issue. The results of the discussion will be used as the basis of a position statement on optimal antimicrobial susceptibility testing in Australia.



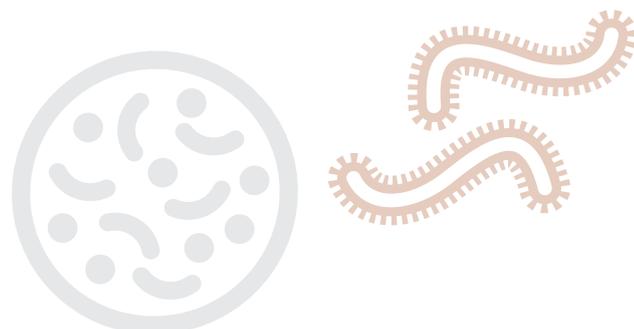


Chapter 7

Conclusions and future developments

Key messages

- The Antimicrobial Use and Resistance in Australia (AURA) Surveillance System has now produced a suite of reports covering antimicrobial resistance (AMR), antimicrobial use (AU) and appropriateness of prescribing.
- These reports demonstrate the benefits of an effective surveillance system and how these data are improving understanding of AU in Australia, and increasing knowledge about the priority organisms that are resistant to antimicrobials.
- AURA 2017 provides more comprehensive data and analyses that, together with other AURA reports, better inform strategies to improve prescribing and prevent and contain AMR.
- The establishment of the National Alert System for Critical Antimicrobial Resistances (CARAlert) provides a mechanism for more timely communication of information about the detection of critical antimicrobial resistances in Australia to enable responsive action.
- Future reporting will be based on consultation with end users to maximise the utility of AURA data.



This chapter provides an overview of the key issues identified and lessons learned from analyses of data for AURA 2017, and the next phases of work in the development of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System.

7.1 Lessons from AURA 2017

Antimicrobial use (AU) in Australian hospitals has continued to decline since the peak usage rate in 2010, with a 2.1% decrease in 2015 compared with 2014, and a 7.6% decrease between 2011 and 2015. Although the antimicrobial usage rate has decreased, the prevalence of AU in hospitals increased from 38.4% of patients being prescribed an antimicrobial in 2014 to 40.5% in 2015. These data, in combination with 21.9% of prescriptions being assessed as inappropriate, and 23.3% not complying with guidelines, provide evidence of the need for further action to improve antimicrobial stewardship.

There was continued improvement in the proportion of surgical prophylaxis prescriptions continuing beyond 24 hours duration, from 41.8% in 2013 down to 27.4% in 2015, but there is more work to be done in this area.

Australia continues to have very high overall rates of community AU compared with a number of comparable countries. In 2015, more than 30 million prescriptions for antimicrobials were dispensed through the Pharmaceutical Benefits Scheme/Repatriation Pharmaceutical Benefits Scheme (PBS/RPBS).

Use of systemic antimicrobials in the community remained high, with 45% of the Australian population being supplied at least one systemic antibiotic through the PBS/RPBS. The rate of prescribing in the community increased from 23.8 defined daily doses (DDDs) per 1,000 inhabitants per day in 2014 to 25.4 DDDs per 1,000 inhabitants per day in 2015. In addition to this high prescribing rate, around 14% of amoxicillin-clavulanate prescriptions were

Area for action

Improve the appropriateness of antimicrobial use for surgical prophylaxis

The use of antimicrobials for surgical prophylaxis is often suboptimal, and antimicrobials are often used for longer than necessary in this setting. The Commission will collaborate with the Royal Australasian College of Surgeons to progress guidance on antimicrobial use in surgical prophylaxis.

prescribed for upper respiratory tract infections where antimicrobials were not indicated. A further 15% of amoxicillin-clavulanate prescriptions were for sinusitis, where antimicrobials are only indicated in specific circumstances.

Of patients who presented to a general practitioner for colds and other upper respiratory tract infections, 60% had an antimicrobial prescribed where no indication was recorded. A large proportion of antimicrobials prescribed were not those recommended by *Therapeutic Guidelines: Antibiotic*. Because many of these prescriptions were unnecessary, and because antimicrobials are frequently used to treat infections for which they provide little or no benefit, efforts to reduce unnecessary prescribing in the community need to be intensified.

Although AURA 2017 has provided a major expansion in national data coverage, there have been few changes in resistance rates compared with AURA 2016. However, noticeable increases were seen in rates of fluoroquinolone resistance in *Escherichia coli* and *Shigella sonnei*, and reduced susceptibility and resistance to benzylpenicillin in *Neisseria meningitidis*. AURA reporting will help to monitor these changes and their effect on patients, and public and private health services.

Area for action

Intensify efforts to reduce unnecessary prescribing in the community

AURA 2017 supports the recommendations of the *Australian Atlas of Healthcare Variation* with regard to antimicrobial dispensing, and the Antimicrobial Stewardship Clinical Care Standard. These include national benchmarks for prescribing antimicrobials, examination by the Pharmaceutical Benefits Advisory Committee (PBAC) of use of amoxicillin-clavulanate, and implementation of antimicrobial stewardship programs in general practice to reduce the use of amoxicillin, amoxicillin-clavulanate and cefalexin.

The AURA National Coordination Unit will work with the Australian Government Department of Health to develop national benchmarks for best-practice prescribing of antimicrobial agents. The Australian Commission on Safety and Quality in Health Care will also work with the PBAC to examine appropriate access to amoxicillin-clavulanate on the Pharmaceutical Benefits Scheme/ Repatriation Pharmaceutical Benefits Scheme, given that most prescribing of this antimicrobial is for conditions that do not require an antimicrobial, or for which amoxicillin alone is recommended in national guidelines.

In *E. coli*, isolates that are resistant to quinolones or that produce extended-spectrum β -lactamases are resistant to third-generation cephalosporins. These strains have been shown to be a continuing and increasing problem in community infections, and they are often multidrug resistant.

Australia has one of the highest rates of vancomycin resistance in *Enterococcus faecium* in the world. Rates of resistance to key antimicrobial agents are very low (<1%) in *E. faecalis*, but high (49–96%) in *E. faecium*. Vancomycin-resistant enterococci continue to be a major healthcare problem in Australia. When enterococci are resistant to vancomycin, only two or three reserved antimicrobials can be used to treat serious infections.

Area for action

Strengthen infection control practices to minimise spread of vancomycin-resistant enterococci

Vancomycin-resistant enterococci are becoming a major healthcare problem in Australia, and only two or three reserved antimicrobials can be used to treat serious infections. Strict adherence to infection control guidelines, and effective cleaning and sterilisation in healthcare facilities is essential.

The Queensland clone of methicillin-resistant *Staphylococcus aureus* (MRSA) has become the dominant clone of community-associated MRSA (CA-MRSA) in Australia. CA-MRSA is now a more common cause of bloodstream infection than healthcare-associated MRSA. Community-onset infections caused by strains of MRSA are likely to fail treatment with the usual β -lactams used by community practitioners, potentially resulting in hospitalisation for treatment with parenteral antimicrobials.

The National Alert System for Critical Antimicrobial Resistances (CARAlert) was established in March 2016 to further strengthen antimicrobial resistance (AMR) surveillance. It is the first nationally coordinated system that supports both collection and communication of

information on confirmed critical antimicrobial resistances (CARs) and potential CAR outbreaks, as close as possible to the time of confirmation. As the data collection develops and the numbers of reports increase to enable meaningful analyses of trends and their implications, these aspects will also be reported on.

CARAlert reports on isolates of *Neisseria gonorrhoeae* that are non-susceptible to ceftriaxone or azithromycin. Strains that are non-susceptible to azithromycin are more common than initially thought. CARAlert data complement state and territory systems that monitor AMR as part of prevention and control strategies for sexually transmissible infections. The emergence of antimicrobial-resistant *N. gonorrhoeae* at the same time as continued increases in disease notifications may lead to treatment failures and disease transmission.

Area for action



Monitor resistant gonococcal infections to inform treatment guidelines

Treatment guidelines for gonococcal infection should be reviewed in light of emerging non-susceptibility to azithromycin. The Australian Commission on Safety and Quality in Health Care will work with the states and territories to provide regular updates on ceftriaxone- or azithromycin-nonsusceptible *Neisseria gonorrhoeae* through the National Alert System for Critical Antimicrobial Resistances (CARAlert), as well as to inform national and local treatment guidelines.

Area for action



Implement actions to control carbapenemase-producing Enterobacteriaceae

Data from the National Alert System for Critical Antimicrobial Resistances (CARAlert) show that carbapenemase-producing Enterobacteriaceae were the most frequently recorded critical antimicrobial resistance between March and December 2016. The IMP-type carbapenemase is now endemic on the Australian eastern seaboard.

The Australian Commission on Safety and Quality in Health Care has published *Recommendations for the Control of Carbapenemase-producing Enterobacteriaceae (CPE): A guide for acute care health facilities* and will work with health service organisations to support timely implementation of these recommendations.

7.2 Next steps for the AURA Surveillance System

Reporting on surveillance is important at the local, state and territory, and national levels. Over time, progressive AURA publications will allow trends to be monitored and inform more specific action in response to AMR. The AURA National Coordination Unit (ANCU) of the Australian Commission on Safety and Quality in Health Care (the Commission) will continue to work with key stakeholders to focus on the analyses and reports that will be of greatest benefit in responding to the gaps identified. This will better inform action at the local, regional, state and territory, and national levels to prevent and contain the spread of AMR. As the volume and comprehensiveness of surveillance data grows, the capacity for more in-depth analysis and epidemiological review of the data will also be improved on and reported.

Throughout 2017, the ANCU will work with laboratory services, and public and private health services to assess the potential to harmonise the

three susceptibility testing systems currently in use in Australia. This work will also consider any longitudinal effect on AURA analyses and reports, as the use of different testing systems can make it difficult to compare resistance rates over time.

As reporting of AURA surveillance data continues to inform patient care and actions at hospital and system levels, it also enables gaps in surveillance coverage to be identified and responded to.

The objective of the AURA Surveillance System is to provide an appropriate balance between information for immediate action and information to monitor progress on preventing and containing AMR over the longer term.

The ANCU will use the resources available to increase data volume and representativeness, and improve data analysis and interpretation. Data definitions and collection methods will be more closely reviewed to improve validity and consistency of approach across the AURA program elements. This will be a focus of work to improve benchmarking and comparability across hospitals and internationally to drive safety and quality improvements.

The ANCU will continue to monitor emerging resistances and changes in patterns of resistance to ensure that these can be rapidly identified and communicated to the states and territories to contain and prevent outbreaks.

Other areas under consideration by the ANCU for further action include:

- Assessing factors that drive variation in AU and prescribing across regions, states and territories
- Improving appropriateness of prescribing in hospitals (particularly for surgical prophylaxis) and the community (particularly for upper respiratory tract infections)
- More detailed analyses of CARAlert data and reporting to support state and territory prevention and control activities.

The Commission has led the development, coordination and oversight of the AURA

Surveillance System. In addition to the alerts and reports to inform policy and program development, the Commission has provided regular updates to the states and territories and the private sector through direct communications and the AURA website to promote active participation. Use of these data will improve prescribing and help to prevent and contain AMR.

7.3 Future AURA reports

The Commission continues to partner with the foundation AMR and AU data collection programs, including the Australian Group on Antimicrobial Resistance, the National Antimicrobial Utilisation Surveillance Program, and the National Antimicrobial Prescribing Survey to improve capacity and participation.

AURA 2017 demonstrates the impact of the Commission's action to improve the diversity and utility of surveillance data, and to embed mechanisms to conduct surveillance. The foundation for future growth and development of AMR and AU surveillance in Australia has been established and allows for further improvements to be made. The ANCU is currently assessing the feasibility and resource implications of integrating additional historical data into the National Passive AMR Surveillance System, which would further improve the capacity for analysing trends and identifying changes in AMR over time.

The frequency and form of future national reports on AU and AMR will be discussed with the states and territories, other key users of these data and reports, and the Australian Government, taking into account the outcomes of the review of governance arrangements for the AURA Surveillance System. Collaboration and cooperation across the public and private sectors in all states and territories will continue to be essential to the reliability and sustainability of the system.



Appendix 1

Data source description

Appendix 1 describes the data sources used for the AURA 2017 report.

A1.1 Antimicrobial use collections

This section provides information on the methods used by each of the data sources for antimicrobial use (AU) used in this report, including information on processes and limitations.

National Antimicrobial Utilisation Surveillance Program

The National Antimicrobial Utilisation Surveillance Program (NAUSP), which began in 2004, focuses on standardised measurement of AU in Australian adult public and private hospitals. NAUSP is administered by the Infection Control Service, Communicable Disease Control Branch, at SA Health. Development and implementation of NAUSP have been an ongoing collaboration between SA Health and the Australian Commission on Safety and Quality in Health Care (the Commission) since 2013.

Hospitals contribute to NAUSP on a voluntary basis. Pharmacy departments of participating hospitals supply NAUSP with aggregate monthly details of antimicrobials issued to individual inpatients and ward imprest supplies (that is, ward stock managed by the pharmacy) using dispensing reports. Hospital occupancy data are

collected in the form of overnight occupied bed days (OBDs).

NAUSP assigns each contributing hospital a unique code. The code is used to report in a de-identified way on usage rates of selected antimicrobials and therapeutic groups.

NAUSP uses standardised usage density rates, based on the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) standards for defined daily doses (DDDs). The denominator is overnight OBDs. Reporting on AU based on DDDs enables assessment and comparison of total hospital use as a rate, and also allows international comparisons.

The NAUSP annual report covers total in-hospital AU data collected from participating hospitals across Australia. Participating hospitals also receive individualised bimonthly reports that provide benchmarking data to inform local quality improvement activities.

Participants

The number of hospitals that contribute to NAUSP has more than doubled since the endorsement of the National Safety and Quality Health Service (NSQHS) Standards in 2011. Participation in NAUSP supports successful implementation of the Preventing and Controlling Healthcare Associated Infection Standard.

In 2015, there were 159 public and private adult acute care hospitals that contributed data to NAUSP. For public hospitals, this represents

approximately half of all facilities categorised by the Australian Institute of Health and Welfare (AIHW) as Principal Referral Hospitals, Public Acute Group A Hospitals, Public Acute Group B Hospitals or Public Acute Group C Hospitals. A growing number of private hospitals are participating in NAUSP; private hospitals will continue to be approached to increase participation.

All Australian states and territories were represented in NAUSP in 2015. Since July 2004, 31 hospitals have contributed continuously, and 13 South Australian hospitals have contributed continuously since the program began there in 2001. In 2015, all Principal Referral Hospitals, and more than 80% of Public Acute Group A and Public Acute Group B Hospitals participated in the program.

The Commission has worked with NAUSP to increase participation and target hospitals that will improve the representativeness of the data, to increase the power of surveillance of AU.

Considerations

The data collected by NAUSP exclude:

- Most topical antimicrobial formulations (except some inhalations), antimycobacterials (except rifampicin), antifungals, antivirals, antiparasitics, and infusor packs of antibacterials for use outside hospital settings
- AU in paediatric hospitals, and paediatric wards and neonatal units within general hospitals – use in this population cannot easily be translated into a standard usage density rate based on the WHO definition of DDDs
- AU for outpatient areas, discharge prescriptions and external services (for example, Hospital in the Home), to ensure that data reflect in-hospital AU
- Antimicrobials issued by pharmacies to individuals and wards classified as specialty areas, such as psychiatric, rehabilitation, dialysis and day-surgery units.

Data provided to NAUSP do not include the indication for which antimicrobials are used, or any patient-specific data. Although some contributing hospitals provide data on ward-by-ward antimicrobial consumption, data for specialist areas (except for intensive care units) have not generally been available.

A comprehensive list of antimicrobials for which data are collected by NAUSP, the ATC classification and the DDD for each route of administration are available from the NAUSP website.

The NAUSP cohort is heavily weighted towards large public hospitals, where antimicrobial stewardship activities are generally well established. In 2015, NAUSP removed restrictions on participation that were based on minimum bed numbers. Participating hospitals are required to meet the criteria for categorisation into one of the eight AIHW peer groups: Principal Referral Hospital; Specialist Women's Hospital; Public Acute Group A, B and C Hospitals; and Private Acute Group A, B and C Hospitals.

Minor discrepancies between annual reports may occur because of data submitted retrospectively by contributing hospitals. To date, NAUSP reports have been confined to use of systemic antibacterials in Australian hospitals. As a result, the term 'antibacterial' rather than 'antimicrobial' is used when referring to the output of analyses of the NAUSP data, and when comparisons are made with data reported by other countries.

Additional issues that need to be considered when interpreting the NAUSP data include the following:

- Participation is voluntary, and smaller facilities in both the public and private sectors, and private facilities generally, are under-represented
- The DDD as defined by WHO occasionally does not match usual daily doses used in Australian hospital clinical practice (see Chapter 3 for more information).

Further information on NAUSP can be found on the NAUSP website.⁸⁶

National Antimicrobial Prescribing Survey

The development and implementation of the National Antimicrobial Prescribing Survey (NAPS) have been an ongoing collaboration between the National Centre for Antimicrobial Stewardship (NCAS) and the Commission since 2013. NAPS is developed and administered by the Guidance Group at Melbourne Health. The Hospital NAPS is the flagship survey of the NCAS.

The Hospital NAPS is a web-based auditing tool and antimicrobial survey program that is conducted annually. The tool is designed to help healthcare facilities assess the quantity and quality of antimicrobial prescribing. Hospitals participate in NAPS voluntarily, and the audit is conducted by a clinician at each site (such as a pharmacist, nurse, infection control practitioner or doctor) following a standardised methodology.

The NCAS has developed guidance to help facilities assess the appropriateness of antimicrobial prescriptions for the survey. This guidance outlines several criteria that must be met (such as guideline concordance, dosing, allergy and microbiology mismatch, and spectrum) for a prescription to be considered appropriate, as well as exclusion criteria when appropriateness is not able to be assessed. The program provides remote support for hospitals without on-site expertise.

Participating hospitals conducted whole-hospital audits using either a point prevalence survey (PPS) or a serial point prevalence survey (sPPS). The sPPS method allows hospitals to repeat PPSs at regular intervals – for example, weekly or fortnightly – until they reach the minimum of 30 antimicrobial prescriptions. Because inpatients could be surveyed more than once using the PPS method, only patients on the first audit day are included in prevalence estimates.

In 2015, the NCAS provided more detailed descriptions of how to conduct a randomised sample survey, including examples of randomisation strategies and suggestions for random number generator tools. This method was recommended for larger hospitals with more than 100 beds without the capacity to conduct a whole-hospital PPS.

Participants

Participation in the Hospital NAPS has grown from 32 pilot sites (30 public and two private) in 2011, when the survey was paper based, to 281 hospitals (213 public and 68 private) in 2015. More information on the growth of the NAPS cohort can be found in Chapter 3 and *AURA 2017: Supplementary data*.

The Hospital NAPS includes representation from all states and territories, and participation by approximately 25% of all public hospitals nationally. In 2015, 80% of Principal Referral Hospitals and 74% of Public Acute Group A Hospitals participated in the survey. Overall, 13.2% of private hospitals participated, including 50% of Group A Hospitals and almost 42% of Group B Hospitals. The greatest increases in participation occurred in inner and outer regional centres. Overall, there was a 13.3% increase in participation compared with the 2014 Hospital NAPS. The Commission will continue to work with the NCAS to increase participation and target hospitals that will improve the representativeness of the data.

Each year, the Hospital NAPS is reviewed and modified to support the requirements of end users. For the 2015 survey, recommendations regarding survey method according to hospital size were included, together with documentation of review or stop date for antimicrobials as a new key indicator.

Considerations

Issues to consider when interpreting the NAPS data include the following:

- Sampling and selection bias – the hospitals included are not a randomised sample because participation by healthcare facilities is voluntary; therefore, the results might not be representative of all Australian hospitals
- Comparison with previous surveys – the ability to directly compare results with those from previous years is limited because of changes in inclusion criteria, methodology and distribution of participating hospitals; also, a small number of hospitals used the 2014 method for the 2015 survey
- Potential for patients to be counted multiple times – for facilities that conducted an sPPS, patients may be counted multiple times if they were still an inpatient on subsequent audit days; this may artificially inflate the prevalence of certain indications or antimicrobials that require longer durations of treatment
- Subjective nature of assessments – individual auditors at each participating facility were responsible for assessing the appropriateness of antimicrobial prescribing and compliance with guidelines, and remote expert assessments were conducted by the NAPS team on request; these assessments are not completely objective and involve some degree of interpretation
- Sample size – some indications for antimicrobials are uncommon; therefore, interpretation is difficult because of small numbers.

Further information on NAPS can be found on the NAPS website.⁸⁷

Pharmaceutical Benefits Scheme

The Australian Government Department of Human Services (DHS) collects data, in the Medicare pharmacy claims database, on antimicrobial dispensing in the community through the Pharmaceutical Benefits Scheme

(PBS) and the Repatriation Pharmaceutical Benefits Scheme (RPBS). Data are submitted to DHS directly by community pharmacies or by eligible patients who have been prescribed a PBS or an RPBS medicine through Medicare service centres.

The Australian Government Department of Health analyses PBS/RPBS data to inform economic analyses and policy development. Comprehensive medicine usage data are required for a number of purposes, including pharmacosurveillance and targeting, and evaluation of initiatives for quality use of medicines. The data are also needed by regulatory and financing authorities, and the pharmaceutical industry.

Data captured by the PBS/RPBS are extensive. Around 30 million prescriptions were supplied for antimicrobials in 2015³², which is approximately 10% of the total PBS and RPBS prescriptions.⁸⁸

Additional data and analysis

As part of the development of the AURA 2017 report, the Commission engaged the University of South Australia to provide an update of the *Antibiotics: PBS/RPBS 2014 report* using PBS/RPBS patient-level pharmacy prescription claims data from 1 January 2015 to 31 December 2015, which was extracted from the Medicare pharmacy claims database. This update includes actual under co-payment prescriptions, but no estimate of private prescriptions. Under co-payment prescriptions are prescriptions priced below the co-payment threshold as defined in the *National Health Act 1953*.

The analyses vary from the *Antibiotics: PBS/RPBS 2015 report* because they include analyses of data for prescriptions and DDDs per 1,000 inhabitants per day for all antibacterials subsidised under the PBS/RPBS. The antibacterials included in the analysis are listed in *AURA 2017: Supplementary data*.

Data for this analysis were retrieved from two sources: the database of the Drug Utilisation Sub Committee (DUSC) of the Pharmaceutical Benefits Advisory Committee, and the Medicare pharmacy claims database.

Drug Utilisation Sub Committee database, February 2017

Aggregated data containing the number of prescriptions and DDDs per 1,000 inhabitants per day for each antibacterial based on date of supply from 1 January 2015 to 31 December 2015 were extracted from the DUSC database. The DUSC database includes an estimate of private prescriptions and under co-payment prescriptions up to April 2012, based on data from a survey of community pharmacies. From April 2012 onwards, it contains actual under co-payment data, but no longer includes estimates of private prescriptions.

Department of Human Services Medicare pharmacy claims database, January 2017

PBS/RPBS data containing patient-level pharmacy prescription claims from 1 January 2015 to 31 December 2015 were extracted from the Medicare pharmacy claims database. The data include actual under co-payment prescriptions, but no estimate of private prescriptions.

Comparison between the DUSC database and the DHS database showed 3% fewer prescriptions in the DHS pharmacy claims data in 2015 than in the DUSC data. This might be because DHS data were requested to provide a valid Statistical Area Level 3 code for the patient and prescribing doctor. DHS data were used for the patient-level analysis.

Yearly data on the number of prescriptions and DDDs per 1,000 people per day were extracted from the DUSC database by date of supply from 1 January 2015 to 31 December 2015, and included all DUSC data that had antibacterial ATC codes.

DHS pharmacy claims data from 1 January 2015 to 31 December 2015 were used to determine:

- The number of antibacterial prescriptions or quantity of antibacterial medicines supplied per person
- The number of people supplied an antibacterial, based on de-identified patient numbers
- The use of antibacterials by patient age group.

The major specialty of the prescriber could not be determined because it was not provided in the DHS pharmacy claims data.

Considerations

Issues that need to be considered when interpreting the PBS/RPBS data include the following:

- Data include antimicrobials dispensed through the PBS and the RPBS; therefore, antimicrobials dispensed from some inpatient and outpatient services, and some community health services may not be captured
- Private prescriptions are not included in this dataset
- These data do not indicate the diagnosis or condition of the patient.

In addition, dispensing through the PBS/RPBS does not necessarily equate to consumption. Antimicrobial consumption can be overestimated because patients may not comply with therapy recommendations.⁸⁹

Further information on the PBS can be found on the PBS website.⁹⁰

MedicineInsight program

NPS MedicineWise currently operates a national program called MedicineInsight, which collects longitudinal, de-identified clinical data from general practices. The data include use of medicines, switching of medicines, indications for prescribing, adherence to guidelines, and pharmacovigilance to support postmarket surveillance of medicine use in primary care,

and to support general practices' improvement in quality use of medicines and medical tests.

The program aims to support changes in prescribing patterns by providing local data to general practices, to allow a better understanding of where there may be variation and opportunity for improvement.

Participation in the MedicinesInsight program is voluntary. An independent data governance committee oversees the project. This report uses data collected on antimicrobials through the program.

Participants

The information presented in this report is based on general practice clinical data collected from volunteer practices recruited to the MedicinesInsight program. The program's dataset is in development, and work is in progress to further develop capabilities and capacity in data analytics and report presentation.

For this report, the results are based on 423 practices and 3,181,923 patients, from the first recording of clinical data in the practices' clinical systems in 2015 until 31 December 2015.

The program has significantly expanded, and a preliminary evaluation has shown that the data are nationally representative.

Considerations

Issues that need to be considered when interpreting the MedicinesInsight data include the following:

- Participation is voluntary; therefore, the general practices included are not a randomised sample
- Data are sourced from medical records, and rely on an appropriate level of completeness and accuracy within the records
- Infrequently attending patients, specialist prescriptions and samples are not included

- Prescribing data can vary from dispensing data, because not all prescriptions are dispensed; therefore, these data may not correlate completely with PBS data.

Further information on the NPS MedicineWise MedicinesInsight program can be found on the MedicinesInsight website.⁹¹

A1.2 Antimicrobial resistance collections

This section provides information on the methods used by each of the data sources for antimicrobial resistance (AMR) used in this report, including information on processes and limitations.

Australian Group on Antimicrobial Resistance

The Australian Group on Antimicrobial Resistance (AGAR) is a collaboration of clinicians and scientists, with involvement from microbiology laboratories in all Australian states and territories. AGAR has been in operation since 1985, with voluntary participation from key microbiology laboratories.

AGAR undertakes targeted surveillance of selected organisms with AMR. Data primarily come from hospitals, but, more recently, capacity has developed to identify resistances present in community settings.

AGAR operates a series of survey programs each year across a range of selected organisms, gathering and reporting information on levels of AMR in species of clinical importance in isolates from blood cultures.⁹² This provides information on AMR in serious infections, and aligns with the European AMR surveillance system (EARS-Net). Microbiology laboratories provide laboratory and demographic data, and isolates to two central AGAR reference laboratories, which undertake molecular testing on selected isolates and

prepare reports on the data for the following three programs:

- Enterobacteriaceae Sepsis Outcome Program (EnSOP); in 2015, *Pseudomonas aeruginosa* and *Acinetobacter* species were added, and the program name was changed to the Gram-negative Sepsis Outcome Program (GNSOP)
- Australian Staphylococcus aureus Sepsis Outcome Program (ASSOP)
- Australian Enterococcus Sepsis Outcome Program (AESOP).

In addition to data on resistances, most participants provide demographic and limited outcome data on each episode of bacteraemia.

Participants

In 2015, 29 laboratories servicing 33 hospitals participated in ASSOP, GNSOP and AESOP. Each of the three collections includes laboratories from all states and territories. There are varying numbers of laboratories in each state and territory, providing services for different types of hospitals. The laboratories are mostly public; a small number of private laboratories participate in each collection.

Considerations

Issues that need to be considered when interpreting the AGAR data include the following:

- Data are not denominator controlled because there is no consensus on an appropriate denominator for these types of surveys
- The surveys are voluntary; institution size, throughput, patient complexity and local AU patterns contribute to the types of resistance likely to be observed
- The program does not currently have capacity to obtain sufficient detailed clinical information to judge the clinical significance of resistance
- The collection requires manual data entry, which can increase the chance of recording errors.

Further information on AGAR can be found on the AGAR website.⁹²

National Neisseria Network

The National Neisseria Network (NNN) is a collaborative association of nine laboratories that contribute to passive laboratory surveillance of the pathogenic *Neisseria* species: *N. gonorrhoeae* and *N. meningitidis*. The NNN conducts two programs: the Australian Gonococcal Surveillance Programme (AGSP) and the Australian Meningococcal Surveillance Programme (AMSP).

Infections caused by *N. gonorrhoeae* and *N. meningitidis* are notifiable diseases under the National Notifiable Diseases Surveillance System (NNDSS). Through this system, notifications are made to state and territory health authorities under the provisions of the relevant public health legislation. Computerised, de-identified unit records of notifications are supplied to DHS daily for collation, analysis, and publication on the department's website and in the quarterly journal *Communicable Diseases Intelligence*.

Australian Gonococcal Surveillance Programme

The AGSP has monitored AMR in clinical isolates of *N. gonorrhoeae* from public and private laboratories across all Australian states and territories since 1981. It is the longest-running national surveillance program for gonococcal AMR in the world.

The NNN laboratories report data on gonococcal susceptibility for an agreed core group of antibacterial agents, on a quarterly basis, to the WHO Collaborating Centre for Sexually Transmitted Diseases. This laboratory is based in Sydney and produces an annual report, published in *Communicable Diseases Intelligence*.⁹³ The antibacterials that are currently routinely surveyed are azithromycin, ceftriaxone, ciprofloxacin, penicillin and spectinomycin.

Although most information gathered and reported by the AGSP is based on resistance surveillance of clinical samples, sentinel surveillance is also undertaken in a very limited number of settings in Australia. The sentinel surveillance activity involves patient follow-up and 'test of cure' cultures following treatment, particularly for oropharyngeal infections and in high-risk populations. This program is important in detecting treatment failure and informing therapeutic strategies.⁹⁴

Considerations

Limitations of the AGSP data used for this report are largely process issues relating to data contributors not fully complying with data quality requirements. An additional possible technical limitation is that susceptibility testing can only be done on specimens sent for gonococcal culture, whereas most cases of gonococcal infection are confirmed based on specimens sent only for nucleic acid testing.

Australian Meningococcal Surveillance Programme

The AMSP, established in 1994⁹⁵, provides a national laboratory-based program for the examination of invasive meningococcal disease caused by *N. meningitidis*.

The AMSP collects data on the strain phenotype (serogroup, serotype and subserotype) and antibacterial sensitivity of invasive meningococcal isolates, as well as nonculture-based laboratory testing (nucleic acid amplification assays and serological examination). The AMSP links the laboratory information with clinical information to provide a comprehensive epidemiological survey.

The incidence of invasive meningococcal disease has significantly and sustainably decreased since 2004, following introduction to the National Immunisation Program in 2003 of a publicly funded serogroup C meningococcal conjugate vaccine. Despite this, invasive meningococcal disease remains a significant public health

concern in Australia, and detailed analysis of locally circulating *N. meningitidis* strains continues to be a priority.

Considerations

Limitations of the AMSP data used for this report are largely process issues relating to data contributors not fully complying with data quality requirements. An additional possible technical limitation is that a small proportion of cases of meningococcal infection are detected using only nucleic acid tests and remain culture negative. Therefore, susceptibility results are not available.

Further information on the NNN can be found on the NNN website.⁹⁶

National Notifiable Diseases Surveillance System

Australia has a well-established *Mycobacterium tuberculosis* surveillance program. Susceptibility testing is undertaken by the Australian Mycobacterium Reference Laboratory Network (AMRLN), and data on resistance are provided to the NNDSS for publication.

The AMRLN started *M. tuberculosis* reporting in 1986. It comprises five state-based *Mycobacterium* reference laboratories, which undertake testing for all states and territories. These laboratories use nucleic acid amplification tests to detect the presence of *M. tuberculosis* complex.

M. tuberculosis is notifiable under the NNDSS. Notifications are made to state and territory health authorities under the provisions of the relevant public health legislation. Computerised, de-identified unit records of notifications are supplied to the Australian Government Department of Health daily for collation, analysis, and publication on the department's website and in the quarterly journal *Communicable Diseases Intelligence*.

Data on *M. tuberculosis* notifications and drug resistance have been publicly available since 1994. Since 2012, *M. tuberculosis* resistance has been reported, together with national notification data, in *Communicable Diseases Intelligence*. The data are also reported annually to the WHO global *M. tuberculosis* surveillance program.

Considerations

Limitations of the NNDSS data used for this report are largely process issues relating to data contributors not fully complying with data quality requirements. In addition, the contributing laboratories have not always used the same susceptibility testing methods, which affects the reliability of historical data.

Further information on the NNDSS and the AMRLN can be found on the Department of Health website (NNDSS annual reports⁹⁷ and a report from the AMRLN⁹⁸).

National Passive AMR Surveillance System (OrgTRx)

The OrgTRx program and associated IT infrastructure were developed by Pathology Queensland and the then Centre for Healthcare Related Infection Surveillance and Prevention. This is the platform for the National Passive AMR Surveillance System.

Contributing laboratories and health services provide the OrgTRx database with susceptibility data for all public patient samples.

Within OrgTRx, a range of filtering and reporting mechanisms allow exclusion of more than one isolate of the same species from the same patient-site combination within a time period. The system also identifies unlikely results, for verification by the originating laboratory.

OrgTRx has the capacity to generate and report on AMR data in the form of:

- Longitudinal datasets for specified organism-antimicrobial combinations

- Cumulative antibiograms showing rates of resistance for a range of organisms from a specified specimen type within a time period
- Tabulations showing the resistance profiles of organism strains isolated during a time period.

OrgTRx can report on combinations of individual units within hospitals or health services, or at a statewide level.

Participants

The national passive AMR surveillance data presented in AURA 2017 have been provided by Pathology Queensland and the Queensland Health Communicable Diseases Branch, which represent individual Queensland hospitals and health services. During 2016, laboratories that provide services to hospitals in the Australian Capital Territory, Monash Health (Victoria), Sydney and South Western Sydney Local Health Districts (New South Wales), Royal Hobart Hospital (Tasmania), Mater Misericordiae Private Hospitals (Queensland) and SA Pathology (South Australia) joined the system, and 2015 data from those sites have been included, where available.

Considerations

Some issues need to be considered when interpreting the national passive AMR surveillance data. Data provided through the system for this report include public hospitals and health services from Queensland (Queensland Health); the Australian Capital Territory; and selected sites in New South Wales, Tasmania and Victoria; as well as private hospitals from Queensland (Mater Queensland). Some public laboratories undertake testing for private facilities and in the community. These data are complemented by data from Sullivan Nicolaides Pathology (SNP), which has provided equivalent data for Queensland private hospitals, the community and aged care homes. SA Pathology (South Australia) has provided data for public hospitals, private hospitals, the community and aged care homes.

Not all antimicrobials are tested against all organisms. Smaller laboratories may test more limited panels, and only test a greater number of antimicrobials for selected isolates.

Sullivan Nicolaides Pathology

SNP is one of the largest members of the Sonic Healthcare group. As part of its practice, SNP collects passive surveillance data on AMR identified through its laboratory network. Similar to OrgTRx, AMR data are held centrally, and a range of filtering and reporting mechanisms allow inclusion or exclusion of multiple isolates from the same patient-site combination within a time period.

Similar to OrgTRx, SNP has the capacity to generate and report AMR data in the form of:

- Longitudinal datasets for specified organism-antimicrobial combinations
- Cumulative antibiograms showing rates of resistance for a range of organisms from a specified specimen type within a time period
- Tabulations showing the resistance profiles of organism strains isolated during a time period.

Participants

SNP data presented in this report are from SNP services provided to private hospitals, aged care homes and general practices.

Considerations

Some of the issues that need to be considered when interpreting the SNP data include the following:

- Data provided through SNP for this report are from private hospitals, aged care homes and general practices based in Queensland and northern New South Wales only; these data are balanced by data from the OrgTRx system, which has provided equivalent data for Queensland public hospitals and health services

- Not all antimicrobials are tested against all organisms, because different laboratories may have their own protocols and undertake selective testing of antimicrobials.

Further information on SNP can be found on the SNP website.⁹⁹

Appendix 2

Priority organisms

The following tables show the priority organisms and their associated antimicrobials for national reporting in targeted surveillance programs.

Priority set 1: Organisms with high public health importance and/or common pathogens where the impact of resistance is substantial in both the hospital and community settings

Species	Core reportable agents
Enterobacteriaceae (mainly <i>Escherichia coli</i> , <i>Klebsiella</i> species and <i>Proteus mirabilis</i>)	Ampicillin, piperacillin-tazobactam, ceftazidime, ceftriaxone/cefotaxime, ciprofloxacin, gentamicin, meropenem
<i>Enterococcus</i> species	Ampicillin, vancomycin, linezolid
<i>Mycobacterium tuberculosis</i>	Isoniazid, ethambutol, pyrazinamide, rifampicin
<i>Neisseria gonorrhoeae</i>	Benzylpenicillin, ceftriaxone/cefotaxime, ciprofloxacin
<i>Neisseria meningitidis</i>	Benzylpenicillin, ceftriaxone/cefotaxime, ciprofloxacin, rifampicin
<i>Salmonella</i> species	Ampicillin, azithromycin, ceftriaxone/cefotaxime, ciprofloxacin
<i>Shigella</i> species	Ampicillin, ciprofloxacin, trimethoprim-sulfamethoxazole, azithromycin
<i>Staphylococcus aureus</i>	Oxacillin (MRSA), ceftazidime (MRSA), ciprofloxacin, clindamycin (including inducible resistance), trimethoprim-sulfamethoxazole, erythromycin, gentamicin, tetracycline, vancomycin, linezolid (if tested), daptomycin (if tested)
<i>Streptococcus pneumoniae</i>	Benzylpenicillin, ceftriaxone/cefotaxime, meropenem

MRSA = methicillin-resistant *Staphylococcus aureus*

Priority set 2: Organisms where the impact of resistance is substantial in hospital settings

Species	Core reportable agents
<i>Acinetobacter baumannii</i> complex	Meropenem
<i>Enterobacter cloacae</i> complex or <i>E. aerogenes</i>	Ceftriaxone/cefotaxime, ciprofloxacin, gentamicin, meropenem
<i>Pseudomonas aeruginosa</i>	Ceftazidime, ciprofloxacin, gentamicin/tobramycin, piperacillin-tazobactam

Priority set 3: Organisms where resistance is a marker of epidemiological resistance and/or use

Species	Core reportable agents
<i>Campylobacter jejuni</i> or <i>C. coli</i>	Ciprofloxacin

Priority set 4: Organisms where resistance will be monitored through passive surveillance, and will be prioritised for targeted surveillance if a signal emerges

Species	Core reportable agents
<i>Clostridium difficile</i>	Moxifloxacin
<i>Haemophilus influenzae</i> type b	Ampicillin, ceftriaxone/cefotaxime, ciprofloxacin
<i>Streptococcus agalactiae</i>	Benzylpenicillin, erythromycin, clindamycin
<i>Streptococcus pyogenes</i>	Benzylpenicillin, erythromycin, clindamycin

Appendix 3

Terminology

A3.1 Acronyms

Acronym	Definition
acNAPS	Aged Care National Antimicrobial Prescribing Survey
ACT	Australian Capital Territory
AGAR	Australian Group on Antimicrobial Resistance
AMR	antimicrobial resistance
AMS	antimicrobial stewardship
ANCU	AURA National Coordination Unit
ATC	Anatomical Therapeutic Chemical
AU	antimicrobial use
AURA	Antimicrobial Use and Resistance in Australia
CA-MRSA	community-associated MRSA
CAR	critical antimicrobial resistance
CARAlert	National Alert System for Critical Antimicrobial Resistances
COPD	chronic obstructive pulmonary disease
CPE	carbapenemase-producing Enterobacteriaceae
DDD	defined daily dose
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ESBL	extended-spectrum β -lactamase
HA-MRSA	healthcare-associated MRSA
HLR	high-level resistance
LLR	low-level resistance
MIC	minimum inhibitory concentration
MRSA	methicillin-resistant <i>Staphylococcus aureus</i>
NAPS	National Antimicrobial Prescribing Survey
NAUSP	National Antimicrobial Utilisation Surveillance Program
NCAS	National Centre for Antimicrobial Stewardship

Acronym	Definition
NPS MedicineWise	National Prescribing Service MedicineWise
NSQHS Standards	National Safety and Quality Health Service Standards
NSW	New South Wales
NT	Northern Territory
OBD	occupied bed day
PBS	Pharmaceutical Benefits Scheme
Qld	Queensland
RPBS	Repatriation Pharmaceutical Benefits Scheme
SA	South Australia
SNP	Sullivan Nicolaides Pathology
Tas	Tasmania
Vic	Victoria
VRE	vancomycin-resistant enterococci
WA	Western Australia
WHO	World Health Organization

A3.2 Common terms

Term	Definition
acquired resistance	Reduction in susceptibility through the acquisition of genes encoding resistance from other bacteria, or through mutation.
aged care home	A special-purpose facility that provides accommodation and other types of support, including assistance with day-to-day living, intensive forms of care, and assistance towards independent living, to frail and aged residents. In AURA 2016, aged care homes were referred to as residential aged care facilities.
antimicrobial	A chemical substance that inhibits or destroys bacteria, parasites, viruses or fungi, and that can be safely administered to humans or animals. In this report, 'antimicrobial' is used: <ul style="list-style-type: none"> • When data on all, or almost all, the classes of agents have been captured in a surveillance program; since this report is confined to systemic antibacterial agents, 'antibacterial' is used when referring to the output of analyses, and when comparisons are made with data reported by other countries • When broadly referring to agents used to treat or prevent infections caused by microbes; the term embraces antibacterial, antifungal, antiviral and antiparasitic agents.
antimicrobial resistance (AMR)	Failure of an antimicrobial to inhibit a microorganism at the antimicrobial concentrations usually achieved over time with standard dosing regimens.
antimicrobial stewardship (AMS)	An ongoing effort by a health service to reduce the risks associated with increasing antimicrobial resistance and to extend the effectiveness of antimicrobial treatments. It may incorporate a broad range of strategies, including monitoring and review of antimicrobial use.
broad-spectrum antimicrobials	A class of antimicrobials that affect many organisms.

Term	Definition
community onset	An organism that is acquired by a patient at least 48 hours before being admitted to a hospital, or specimens collected in the community, outpatient clinics or emergency departments.
defined daily dose (DDD)	The average dose per day to treat the main indication for an average adult patient, as defined by the World Health Organization.
extended-spectrum β -lactamase	An enzyme that is produced by some gram-negative bacteria. Bacteria that produce these enzymes are usually found in the bowel and urinary tract, and are considered to be multidrug-resistant organisms because they are resistant to a large number of antimicrobials.
hospital	All public, private, acute and psychiatric hospitals; free-standing day hospital facilities; and alcohol and drug treatment centres. It includes hospitals specialising in dentistry, ophthalmology and other acute medical or surgical care. It may also include hospitals run by the Australian Defence Force and corrections authorities, and those in Australia's offshore territories. It excludes outpatient clinics and emergency departments.
hospital onset	An organism that is acquired by a patient at least 48 hours after being admitted to a hospital.
hospital peer group	Grouping of Australian public and private hospitals according to a classification system developed by the Australian Institute of Health and Welfare. Hospitals are assigned to peer groups based on the type and nature of the services they provide. Peer grouping of hospitals supports valid comparisons that reflect the purpose, resources and role of each hospital. The peer groups included in the analyses for AURA 2017 are: <ul style="list-style-type: none"> • Principal Referral Hospital • Specialist Women's Hospital • Public Acute Group A Hospital • Public Acute Group B Hospital • Public Acute Group C Hospital • Private Acute Group A Hospital • Private Acute Group B Hospital • Private Acute Group C Hospital.
intrinsic resistance	Natural lack of susceptibility to the antimicrobial as used for treatment.
National Safety and Quality Health Service (NSQHS) Standards	Standards developed by the Australian Commission on Safety and Quality in Health Care to drive the implementation of safety and quality systems, and improve the quality of health care in Australia. The NSQHS Standards provide a nationally consistent statement about the level of care consumers can expect from health service organisations.
occupied bed days (OBDs)	The total number of bed days of all admitted patients accommodated during the reporting period, taken from a count of the number of inpatients at about midnight each day.
passive surveillance	Data collection designed for a broader purpose, but where a subset of the data can be used for secondary analysis. In this report, it refers to broader collections from which data on antimicrobial use and resistance can be extracted.
Pharmaceutical Benefits Scheme (PBS)	An Australian Government program that subsidises medicines.
Principal Referral Hospital	Major city hospitals with more than 20,000 acute casemix-adjusted separations per year, and regional hospitals with more than 16,000 acute casemix-adjusted separations per year.
Repatriation Pharmaceutical Benefits Scheme (RPBS)	An Australian Government program that subsidises medicines for veterans.

Term	Definition
targeted surveillance	Data collection designed for a specific and targeted purpose. In this report, it refers to collections specifically designed for the surveillance of antimicrobial-resistant organisms.
therapeutic group or class	Categorisation of drugs that have similar chemical structure and spectrum.
topical (medication)	A medication that is applied to body surfaces such as the skin or mucous membranes; includes creams, foams, gels, lotions and ointments.

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