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Australian Group on Antimicrobial Resistance (AGAR) Australian Enterococcal Sepsis Outcome Programme (AESOP) Annual Report 2016

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on behalf of the Australian Group on Antimicrobial Resistance

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Australian Group on Antimicrobial Resistance (AGAR) Australian Enterococcal Sepsis Outcome Programme (AESOP) Annual Report 2016

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Abstract

From 1st January to 31st December 2016, 32 institutions around Australia participated in the Australian Enterococcal Sepsis Outcome Programme (AESOP). The aim of AESOP 2016 was to determine the proportion of enterococcal bacteraemia isolates in Australia that were antimicrobial resistant, and to characterise the molecular epidemiology of the *E. faecium* isolates. Of the 1,058 unique episodes of bacteraemia investigated, 95.2% were caused by either *E. faecalis* (56.2%) or *E. faecium* (39.0%) Ampicillin resistance was detected in 0.2% of *E. faecalis* and in 91.5% of *E. faecium*. Vancomycin non-susceptibility was reported in 0.3% and 47.7% of *E. faecalis* and *E. faecium* respectively. Overall, 49.3% of *E. faecium* harboured *vanA* or *vanB* genes. For the *vanA/B* positive *E. faecium* isolates, 55.2% harboured *vanB* genes and 42.8% *vanA* genes, 2% harboured *vanA* and *vanB* genes. The percentage of *E. faecium* bacteraemia isolates resistant to vancomycin in Australia is significantly higher than that seen in most European countries. *E. faecium* consisted of 48 multilocus sequence types (STs) of which 90.2% of isolates were classified into 13 major STs containing 5 or more isolates. All major STs belong to clonal cluster (C) 17, a major hospital-adapted polyclonal *E. faecium* cluster. Four of the 6 predominant STs (ST17, ST796, ST80 and ST203) were found across most regions of Australia. The most predominant clone ST1421 (previously known as M-type 1) does not have a *pstS* housekeeping gene and was found in NSW, the ACT and Victoria. This clone was first described in ASSOP 2015. Overall, 74% of isolates belonging to the 6 predominant STs harboured *vanA* or *vanB* genes. The AESOP 2016 has shown enterococcal bacteraemias in Australia are frequently caused by polyclonal ampicillin-resistant high-level gentamicin resistant *vanA* or *vanB E. faecium* which have limited treatment options.

Keywords: Australian Group on Antimicrobial Resistance (AGAR); antimicrobial resistance surveillance; *Enterococcus faecium*, *Enterococcus faecalis*, Vancomycin Resistant Enterococci (VRE), Bacteraemia

Background

Globally, enterococci are thought to account for approximately 10% of all bacteraemias, and in North America and Europe is the fourth and fifth leading cause of sepsis respectively.[1,2] Although, in the 1970s healthcare-associated enterococcal infections were primarily due to *Enterococcus faecalis*, there has been a steadily increasing prevalence of *E. faecium* nosocomial infections.[3-5] Worldwide the increase in nosocomial *E. faecium* infections has primarily been due to the expansion of polyclonal hospital-adapted clonal complex (CC) 17 strains. While innately resistant to many classes of antibiotics, *E. faecium* has demonstrated a remarkable capacity to evolve new antimicrobial resistances. In 2009, the Infectious Diseases Society of

America highlighted *E. faecium* as one of the key problem bacteria or ESKAPE (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter species*) pathogens requiring new therapies.[6]

The Australian Group on Antimicrobial Resistance (AGAR) is a network of laboratories located across Australia that commenced surveillance of antimicrobial resistance in *Enterococcus* species in 1995.[7] In 2011, AGAR commenced the Australian Enterococcal Sepsis Outcome Programme (AESOP).[8] The objective of AESOP 2016 was to determine the proportion of *E. faecalis* and *E. faecium* bacteraemia isolates demonstrating antimicrobial resistance with particular emphasis on:

1. Assessing susceptibility to ampicillin

2. Assessing susceptibility to glycopeptides

3. Molecular epidemiology of *E. faecium*

Methodology

Participants

32 laboratories from all 8 Australian states and territories.

Collection Period

From 1st January to 31st December 2016, the 32 laboratories collected all enterococcal species isolated from blood cultures. Enterococci with the same species and antimicrobial susceptibility profiles isolated from a patient's blood culture within 14 days of the first positive culture were excluded. A new enterococcal sepsis episode in the same patient was recorded if it was confirmed by a further culture of blood taken more than 14 days after the initial positive culture. Data were collected on age, sex, date of admission and discharge (if admitted), and mortality at 30 days from date of blood culture collection. To avoid interpretive bias, no attempt was made to assign attributable mortality. Each episode of bacteraemia was designated as "hospital-onset" if the first positive blood culture(s) in an episode was collected >48 hours after admission.

Laboratory Testing

Enterococcal isolates were identified to the species level by the participating laboratories using one of the following methods: API 20S (bioMérieux), API ID32Strep (bioMérieux), Vitek2® (bioMérieux), Phoenix™ (BD), matrix-assisted laser desorption ionization (MALDI) Biotyper (Bruker Daltonics), Vitek-MS (bioMérieux), PCR, or conventional biochemical tests. Antimicrobial susceptibility testing was performed by using the Vitek2® (bioMérieux, France) or the Phoenix™ (BD, USA) automated microbiology systems according to the manufacturer's instructions. Minimum inhibitory concentration (MIC) data and isolates were referred to the Antimicrobial Resistance and Infectious Diseases (AMRID) Research Laboratory, at Murdoch University. Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints were utilised for interpretation.[9,10] Isolates with either a resistant or an intermediate category were classified as non-susceptible. Linezolid and daptomycin non-susceptible isolates and selected vancomycin susceptible isolates were retested by Etest® (bioMérieux, France) using the Mueller-Hinton agar recommended by the manufacturer. *E. faecalis* ATCC® 29212 was used as the control strain. Molecular testing was performed by whole genome sequencing using the MiSeq® platform (Illumina, San Diego, USA). Sequencing results were analysed using the Nullarbor pipeline.[11]

A chi-square test for comparison of 2 proportions was performed and 95% confidence intervals (95% CI) were determined using MedCalc for Windows, version 12.7 (MedCalc Software, Ostend Belgium).

Approval to conduct the prospective data collection was given by the research ethics committee associated with each participating laboratory.

Results

From 1st January to 31st December 2016, 1,058 unique episodes of enterococcal bacteraemia were identified. Although 7 *Enterococcus* species were identified, 56.2% (595 isolates) were *E. faecalis* and 39.0% (413 isolates) were *E. faecium*. Fifty enterococci were identified either as *E. casseliflavus* (25 isolates), *E. gallinarum* (11), *E. avium* (8), *E. hirae* (3) and *E. raffinosus* (3).

A significant difference was seen in patient sex (p<0.0001) with 701 (66.3%) being male (95% CI, 63.4– 69.2). The average age of patients was 64 years ranging from 0 – 101 years with a median age of 68 years. The majority of episodes 53.0% (561/1,058) were hospital-onset (95% CI, 49.9 – 56.0). However, a significant difference (p<0.0001) was seen between *E. faecium* and E. *faecalis*, with 72.4% (95% CI, 67.8 – 76.7) of *E. faecium* episodes being hospital-onset compared to 31.3% (95% CI, 28.0 – 35.2) for *E. faecalis*. All-cause mortality at 30 days where data was known was 19.3% (95% CI, 16.8 – 22.0). There was a significant difference (p<0.0001) in mortality between *E. faecalis* and *E. faecium* episodes 12.9% vs 27.2% respectively, and between vancomycin susceptible and vancomycin non-susceptible *E. faecium* episodes 17.0% vs 28.3% respectively (p=0.0008).

E. faecalis Phenotypic Susceptibility Results

Apart from erythromycin, tetracycline, ciprofloxacin and high-level gentamicin, acquired resistance was rare amongst *E. faecalis* (Table 1). Ampicillin resistance was detected in one isolate and 2 isolates were vancomycin non-susceptible. Twenty-two (3.7%) *E. faecalis*, were initially reported as linezolid non-susceptible (CLSI breakpoint >2 mg/L). However, by Etest® seven of the 22 isolates had a linezolid MIC of ≤2 mg/L and were therefore considered linezolid susceptible. Fifteen isolates with an MIC of 4 mg/L although non-susceptible by CLSI guidelines were considered susceptible by EUCAST guidelines. Two isolates had an MIC of 8 mg/L and were non-susceptible. All isolates were susceptible to teicoplanin and daptomycin.

E. faecium Phenotypic Susceptibility Results

The majority of *E. faecium* were non-susceptible to multiple antimicrobials (Table 2). Most isolates were non-susceptible to ampicillin, erythromycin, tetracycline, ciprofloxacin, nitrofurantoin and high-level gentamicin. Overall, 197 (47.7%) were phenotypically vancomycin non-susceptible (MIC >4 mg/L). Seventy-eight (18.9%) and eighty-one (19.6%) isolates were teicoplanin non-susceptible by CLSI and EUCAST guidelines respectively. Four (1.0%) isolates were initially reported as linezolid non-susceptible (CLSI breakpoint >2 mg/L). However, by Etest® 2 of the 4 isolates had a linezolid MICs of 2 mg/ and 1.5mg/L and therefore were considered susceptible. Two isolates had MICs of 4mg/L which was considered susceptible by EUCAST guidelines but non-susceptible by CLSI guidelines.

Genotypic Vancomycin Susceptibility Results

vanA/vanB PCR results were available for 302 of the 595 *E. faecalis* isolates. Three of the 302 isolates harboured a *vanB* gene and one isolate harboured a *vanA* gene.

The presence of *vanA*/*B* genes was determined by PCR or whole genome sequencing on 408 of the 413 *E. faecium* isolates. Overall, 201 (49.3%) of the 408 isolates harboured a *vanA* and/or *vanB* gene. Eighty-three of the vancomycin non-susceptible *E. faecium* isolates harboured *vanA* (Vitek® vancomycin MIC >4mg/). A further 110 *E. faecium* vancomycin non-susceptible isolates harboured *vanB*). Four isolates harboured *vanA* and vanB genes.

vanA or *vanB* genes were detected in 6 vancomycin susceptible *E. faecium* isolates. Three isolates harboured *vanA* (Vitek® vancomycin MIC ≤ 0.5mg/L [one isolate], MIC = 1 mg/L [2 isolates], teicoplanin ≤1mg/L [3 isolates]). Three isolates harboured *vanB* (Vitek® vancomycin MIC = 1 mg/L, 2mg/L and 4mg/L)

Table 1: The number and proportion of E. faecalis non-susceptible to ampicillin and the non-β-lactam antimicrobials, Australia, 2016

Antimicrobial	Tested	Breakpoint (mg/L)	Non-Susceptible	
			n	%
Ampicillin	592	>8*	1	0.2
		>4†	1	0.2
Vancomycin	592	>4‡	2	0.3
Erythromycin	579	>0.5*	522	90.2
Tetracycline/Doxycycline	579	>4*	384	71.0
Ciprofloxacin	559	>1*	86	15.4
Daptomycin	542	>4*	0	0
Teicoplanin	558	>8*	0	0
		>2†	0	0
Linezolid	591	>2*	17	2.9
		>4†	2	0.3
Nitrofurantoin	591	>32*	3	0.5
		>64†	0	0
High Level Gentamicin	589	>128†	143	24.3

*CLSI non-susceptible breakpoint

†EUCAST non-susceptible breakpoint

‡CLSI and EUCAST non-susceptible breakpoint

E. faecium Molecular Epidemiology

Of the 413 episodes, 400 *E. faecium* isolates were available for typing by whole genome sequencing. The 400 isolates were classified into 48 sequence types (STs) including 13 STs with 5 or more isolates (Table 3). A clone first described in AESOP 2015 (non-typable pstS housekeeping gene absent) was re-named M-type 1. In 2016, there were four M-type single locus variants (M-type 1 [64 isolates], M-type 2 [5 isolates], M-type 3 [15 isolates] and M-type 4 [1 isolate]). These have now been classified as ST1421, ST1422, ST1424 and ST1423 respectively. Of the 35 STs with <5 isolates, 30 had only one isolate. Overall, 359 (89.8%) of the 400 isolates were grouped into the 13 major STs. Using eBURST, the 13 STs were grouped into CC 17.

Geographical distribution of the STs varied (Table 3). For the 6 most prominent STs, ST1421 (64 isolates) was identified in the Australian Capital Territory, New South Wales and Victoria; ST17 (59 isolates) in all regions except Western Australia and the Australian Capital Territory; ST80 (51 isolates) found in all regions except the Northern Territory and Tasmania; ST555 (39 isolates) across most of Australia except the Australian Capital Territory, New South Wales and Victoria; and ST203 (39 isolates) found in all regions except the Northern Territory.

vanA was detected in seven major STs (85 isolates, ST1421, ST17, ST80, ST555, ST203, ST1424, and ST78). *vanB* was detected in 9 major STs (111 isolates, ST1421, ST17, ST796, ST80, ST555, ST203, ST78, and ST262) (Table 4). ST780 harboured vanA and vanB genes. One minor ST (1 isolate) harboured vanB genes and one minor ST (1 isolate) harboured vanA and vanB genes.

Table 2: The number and proportion of *E. faecium* non-susceptible to ampicillin and the non-β-lactam antimicrobials, Australia, 2016

Antimicrobial	Tested	Breakpoint (mg/L)	Non-Susceptible	
			n	%
Ampicillin	412	>8*	377	91.5
		>4†	380	92.2
Vancomycin	413	>4‡	197	47.7
Erythromycin	410	>0.5*	389	94.9
Tetracycline/Doxycycline	411	>4*	256	62.3
Ciprofloxacin	404	>1*	372	92.1
Teicoplanin	413	>8*	78	18.9
		>2†	81	19.6
Linezolid	399	>2*	2	0.5
		>4†	0	0
Nitrofurantoin	398	>32*	319	77.8
		>64†	196	47.8
High Level Gentamicin	385	>128*	230	59.7

*CLSI non-susceptible breakpoint

†EUCAST non-susceptible breakpoint

‡CLSI and EUCAST non-susceptible breakpoint

Discussion

Enterococci are intrinsically resistant to a broad range of antimicrobials including the cephalosporins and sulphonamides. By their ability to acquire additional resistance through the transfer of plasmids and transposons and to disseminate easily in the hospital environment enterococci have become difficult to treat and provide major infection control challenges.

As the AGAR programs are similar to those conducted in Europe (http://www.ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/database.aspx) comparison of Australia antimicrobial resistance data with other countries is possible.

In the 2016 European Centre for Disease Prevention and Control and Prevention (ECDC) Enterococci surveillance program, the European Union/European Economic Area (EU/EEA) population-weighted mean percentage of *E. faecium* resistant to vancomycin was 11.8% (95% CI, 11 – 13), ranging from 0.0% in Estonia (95% CI, 0 – 6), Finland (95% CI, 0 – 1), Iceland, (95% CI, 0 – 21) Luxembourg (95% CI, 0 – 11) and Slovenia (95% CI, 0 – 3) to 45.8% (95% CI, 31 – 63) in Cyprus. (http://ecdc.europa.eu/en/publications/Publications/antimicrobial-resistance-surveillance-europe-2016.pdf).

In AESOP 2016, approximately 40% of enterococcal bacteraemia were due to *E. faecium* of which 47.7% (95% CI, 42.8 – 52.6) were phenotypically vancomycin non-susceptible by Vitek2® or Phoenix™. However, 49.3% of *E. faecium* isolates tested (201/408) harboured *vanA/vanB* genes, of which 55% were *vanB*. Overall, 21.6% (88/408) of *E. faecium* isolates harboured a *vanA* gene. There has been a significant increase in *vanA E. faecium* in Australia over the last 3 surveys

Table 3: The number and proportion of major Enterococcus faecium sequence types, Australia, 2016, by region

ST	ACT		NSW		NT		Qld		SA		Tas		Vic		WA		Aus	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
1,421	15	68.2	40	34.8									9	8.3			64	16.0
17	1	4.5	5	4.3			22	52.4	2	4.9			8	7.3	21	39.6	59	14.8
796			2	1.7	1	25.0	1	2.4	2	4.9	6	42.9	45	41.3			57	14.3
80	3	13.6	19	16.5			3	7.1	1	2.4			15	13.8	10	18.9	51	12.8
555					2	50.0	1	2.4	20	48.8	3	21.4			13	24.5	39	9.8
203	1	4.5	6	5.2			4	9.5	3	7.3	1	7.1	10	9.2	1	1.9	26	6.5
1,424			15	13.0													15	3.8
78			7	6.1			6	14.3									13	3.3
262									12	29.3							12	3.0
117			4	3.5			1	2.4			1	7.1			1	1.9	7	1.8
192											2	14.3	4	3.7			6	1.5
18			1	0.9			1	2.4					1	0.9	2	3.8	5	1.3
1,422			5	4.3													5	1.3
Other	**2**	**9.1**	**11**	**9.6**	**1**	**25.0**	**3**	**7.1**	**1**	**2.4**	**1**	**7.1**	**17**	**15.6**	**5**	**9.4**	**41**	**10.3**
Total	22	100	115	100	4	100	42	100	41	100	14	100	109	100	53	100	400	100

*The pstS housekeeping gene is absent in the M-type isolates. ACT = Australian Capital Territory; NSW = New South Wales; NT = Northern Territory; Qld = Queensland; SA = South Australia; Tas1 = Tasmania; Vic = Victoria; WA = Western Australia; Aus = Australia

Table 4: The number and proportion of major Enterococcus faecium sequence types harbouring vanA/B genes, Australia, 2016

ST	n	vanA		vanB		vanA and vanB		Not Detected	
		n	%	n	%	n	%	n	%
1,421	64	51	79.7	1	1.6			12	18.8
17	59	1	1.7	4	6.8			54	91.5
796	57			55	96.5			2	3.5
80	51	17	33.3	5	9.8	2	3.9	27	52.9
555	39	1	2.6	17	43.6			21	53.8
203	26	3	11.5	14	53.8			9	34.6
1,424	15	11	73.3					4	26.7
78	13	1	7.7	11	84.6			1	7.7
262	12			2	16.7			10	83.3
117	7							7	100
192	6							6	100
18	5							5	100
1,422	5							5	100
Other	41			1	2.4	1	2.4	39	95.1
Total	400	85	21.3	110	27.5	3	0.8	202	50.5

*The pstS housekeeping gene is absent in the M-type isolates.

from 6% (8/310) in AESOP 2013, 9.5% (35/370) in 2014 and 20.7% (82/397) in 2015.[12,13] The majority of *E. faecium* isolates were also non-susceptible to multiple antimicrobials including ampicillin, erythromycin, tetracycline, ciprofloxacin and high level gentamicin. In AESOP 2011[14], 2013[12], 2014[13] and 2015[15] 37.0%, 48.6%, 51.1% and 49.3% of *E. faecium* respectively harboured *vanA/vanB* confirming the incidence of vancomycin resistant *E. faecium* bacteraemia in Australia is a significant problem.

Three (2.7%) of the 110 *vanB E. faecium* and 3 of the *vanA E. faecium* isolates had a vancomycin MIC at or below the CLSI and the EUCAST susceptible breakpoint (≤4 mg/L) and therefore would not have been identified using routine phenotypic antimicrobial susceptibility methods.

By whole genome sequencing, *E. faecium* was shown to be very polyclonal, consistent with the known plasticity of the enterococcal genome. The 13 major *E. faecium* STs formed part of CC17, a global hospital-derived lineage that has successfully adapted to hospital environments. CC17 is characteristically ampicillin and quinolone resistant and subsequent acquisition of *vanA* – or *vanB* – containing transposons by horizontal transfer in CC17 clones has resulted in VRE with pandemic potential.

In AESOP 2016, six *E. faecium* STs predominated: ST1421 (of which 79.7% of isolates harboured *vanA* genes, 1.6% *vanB* genes); ST17 (6.8% *vanB*, 1.7% *vanA)* ; ST796 (96.5% *vanB*); ST80 (33.3% *vanA,* 9.8% *vanB,* 3.9% *vanA* and *vanB*), ST555 (43.6% *vanB*, 2.6% *vanA*) and ST203 (53.8% *vanB*, 11.5% *van*).

Conclusions

The AESOP 2016 study has shown, although predominately caused by *E. faecalis,* enterococcal bacteraemia in Australia is frequently caused by ampicillin-resistant high-level gentamicin-resistant *vanB E. faecium*. Furthermore the percentage of *E. faecium* bacteraemia isolates resistant to vancomycin in Australia is significantly higher than that seen in almost all European countries. Although the *vanB* operon continues to be the predominant genotype, the number of *vanA E. faecium* identified in AESOP 2016 has increased when compared to AESOP 2013, 2014 and 2015. In addition to being a significant cause of healthcare-associated sepsis, the emergence

of multiple multi-resistant hospital-adapted *E. faecium* strains has become a major infection control issue in Australian hospitals. Further studies on the enterococcal genome will contribute to our understanding of the rapid and ongoing evolution of enterococci in the hospital environment and assist in preventing their nosocomial transmission.

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Reference

1. Pinholt M, Ostergaard C, Arpi M et al. Incidence, clinical characteristics and 30-day mortality of enterococcal bacteraemia in Denmark 2006-2009: a population-based cohort study. *Clin Microbiol Infect* 2014;20(2):145-151.

2. Deshpande LM, Fritsche TR, Moet GJ et al. Antimicrobial resistance and molecular epidemiology of vancomycin-resistant enterococci from North America and Europe: a report from the SENTRY antimicrobial surveillance program. *Diagn Microbiol Infect Dis* 2007; 58: 163-70.

3. Murray BE. The life and times of the Enterococcus. *Clin Microbiol Rev* 1990; 3: 46-65.

4. Simonsen GS, Smabrekke L, Monnet DL et al. Prevalence of resistance to ampicillin, gentamicin and vancomycin in Enterococcus faecalis and Enterococcus faecium isolates from clinical specimens and use of antimicrobials in five Nordic hospitals. *J Antimicrob Cchemother* 2003; 51: 323-31.

5. Treitman AN, Yarnold PR, Warren J et al. Emerging incidence of Enterococcus faecium among hospital isolates (1993 to 2002). *J clin*

Microbiol 2005; 43: 462-3.

6. Boucher HW, Talbot GH, Bradley JS et al. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. *Clin Infect Dis* 2009; 48: 1-12.

7. Christiansen KJ, Turnidge JD, Bell JM et al. Prevalence of antimicrobial resistance in Enterococcus isolates in Australia, 2005: report from the Australian Group on Antimicrobial Resistance. *Commun Dis Intell* 2007; 31: 392-7.

8. Coombs GW, Daley D, Pearson JC et al. A change in the molecular epidemiology of vancomycin resistant enterococci in Western Australia. *Pathol* 2014; 46: 73-5.

9. CLSI. Performance standards for antimicrobial susceptibility testing. *Twenty-fourth informational supplement M100-S24*. Villanova, PA, USA, 2014.

10. European Committee on Antimicrobial Susceptibility Testing. Clinical breakpoints. 2015.

11. Seemann T, Goncalves da Silva A, Bulach DM, Schultz MB, Kwong JC, Howden BP. Nullarbor. San Francisco; Github. [Accessed: 03 Jun 2016]. Available from: https://github.com/tseemann/nullarbor

12. Coombs GW, Pearson JC, Daly DA et al. Australian Enterococcal Sepsis Outcome Programme annual report, 2013. *Commun Dis Intell* 2014; 38: E320-6.

13. Coombs GW, Daley DA, Thin Lee Y, Pang S, Pearson JC, Robinson JO, Johnson PD, Kotsanas D, Bell JM, Turnidge JD; Australian Group on Antimicrobial Resistance.Australian Group on Antimicrobial Resistance Australian Enterococcal Sepsis Outcome Programme annual report, 2014.*Commun Dis Intell* Q Rep. 2016 Jun 30;40(2):E236-43.

14. Coombs GW, Pearson JC, Daley DA et al. Molecular epidemiology of enterococcal bacteremia in Australia. *J Clin Mmicrobiol* 2014; 52: 897-905.

15. Coombs GW, Daley DA, Lee YT, Pang S, Bell JM, Turnidge JD for the Australian Group on Antimicrobial Resistance. Australian Group on Antimicrobial Resistance (AGAR) Australian Enterococcal Sepsis Outcome Programme (AESOP) Annual Report 2015 - submitted for publication. *Commun Dis Intell*