Australian Group on Antimicrobial Resistance (AGAR) Australian Enterococcal Sepsis Outcome Programme (AESOP) Annual Report 2017

Geoffrey W Coombs, Denise A Daley, Yung Thin Lee, Dr Stanley Pang on behalf of the Australian Group on Antimicrobial Resistance
Annual report

Australian Group on Antimicrobial Resistance (AGAR) Australian Enterococcal Sepsis Outcome Programme (AESOP) Annual Report 2017

Geoffrey W Coombs, Denise A Daley, Yung Thin Lee, Dr Stanley Pang on behalf of the Australian Group on Antimicrobial Resistance

Abstract

From 1 January to 31 December 2017, 36 institutions around Australia participated in the Australian Enterococcal Sepsis Outcome Programme (AESOP). The aim of AESOP 2017 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 1,137 unique episodes of bacteraemia investigated, 95.2% were caused by either E. faecalis (52.9%) or E. faecium (42.3%). Ampicillin resistance was not detected in E. faecalis but in 89.6% of E. faecium. Vancomycin non-susceptibility was reported in 0.3% and 47.0% of E. faecalis and E. faecium respectively. Overall 50.9% of E. faecium harboured vanA or vanB genes. For the vanA/B positive E. faecium isolates, 49.6% harboured vanB genes and 49.2% vanA genes; 1.2% 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 76 multilocus sequence types (STs) of which 77% of isolates were classified into nine major STs containing ten or more isolates. All major STs belong to clonal cluster (CC) 17, a major hospital-adapted polyclonal E. faecium cluster. Seven of the nine predominant STs (ST80, ST1421, ST17, ST296, ST555, ST203 and ST18) were found across most regions of Australia. The most predominant clone was ST17 which was identified in all regions except the Australian Capital Territory, the Northern Territory and Tasmania. Overall 60.7% of isolates belonging to the nine predominant STs harboured vanA or vanB genes. The AESOP 2017 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 are 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 17 (CC17) 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 baumanii, Pseudomonas aeruginosa, and Enterobacter species) pathogens requiring new therapies.

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. In 2011, AGAR commenced the Australian Enterococcal Sepsis Outcome Programme (AESOP). The objective of AESOP 2017 was to determine the proportion of *E. faecalis* and *E. faecium* bacteraemia isolates demonstrating antimicrobial resistance with particular emphasis on:

- Assessing susceptibility to ampicillin
- Assessing susceptibility to glycopeptides
- Molecular epidemiology of *E. faecium*

**Methodology**

**Participants**

Thirty-six laboratories from all eight Australian states and mainland territories.

**Collection Period**

From 1 January to 31 December 2017, the 36 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, France), API ID32Strep (bioMérieux), Vitek2® (bioMérieux), Phoenix™ (Becton Dickinson, USA), matrix-assisted laser desorption ionization (MALDI) Biotyper (Bruker Daltonics), Vitek-MS (bioMérieux), polymerase chain reaction (PCR), or conventional biochemical tests. Antimicrobial susceptibility testing was performed by using the Vitek2® or the Phoenix™ 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. Isolates with either a resistant or an intermediate category were classified as non-susceptible. Linezolid and daptomycin non-susceptible isolates and vancomycin susceptible isolates which harboured vanA or vanB genes were retested by Etest® (bioMérieux) 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 (WGS) using the MiSeq® platform (Illumina, San Diego, USA). Sequencing results were analysed using the Nullarbor pipeline.

A chi-squared test for comparison of two 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 1 January to 31 December 2017, a total of 1,137 unique episodes of enterococcal bacteraemia were identified. Although nine Enterococcus species were identified, 52.9% (602 isolates) were E. faecalis and 42.3% (481 isolates) were E. faecium. Fifty-four enterococci were identified either as E. casseliflavus (19 isolates), E. gallinarum (14 isolates), E. avium (9 isolates), E. durans (4 isolates), E. raffinosis (4 isolates) E. hirae (2 isolates), E. saccharolyticus (1 isolate) or Enterococcus species (unidentified) (1 isolate).

A significant difference was seen in patient sex ($p<0.001$) with 731 (64.3%) being male (95% CI, 61.3–67.1). The average age of patients was 63 years ranging from 0–99 years with a median age of 67 years. The majority of episodes, 53.9% (613/1,137), were community-onset (95% CI, 51.0–56.8). However, a significant difference ($p<0.001$) in place of onset was seen between E. faecium and E. faecalis, with only 29.9% (95% CI, 25.8–34.2) of E. faecium episodes being community-onset compared to 71.1% (95% CI, 67.3–74.7) for E. faecalis. All-cause mortality at 30 days where data was known was 20.0% (95% CI, 17.5–22.7). There was a significant difference ($p<0.001$) in mortality between E. faecalis and E. faecium episodes, 14.1% vs 27.3% respectively, but not between vancomycin-susceptible and vancomycin non-susceptible E. faecium episodes, 25.9% vs 27.7% respectively ($p=0.7$).

E. faecalis Phenotypic Susceptibility Results

Apart from erythromycin, tetracycline, ciprofloxacin and high-level gentamicin, acquired resistance was rare amongst E. faecalis (Table 1). Two isolates were vancomycin non-susceptible. Ampicillin resistance was not detected. Sixteen (2.7%) E. faecalis were initially reported as linezolid non-susceptible (CLSI breakpoint >2 mg/L). However by Etest® nine of the 16 isolates had a linezolid MICs of ≤2 mg/L and therefore were considered susceptible. Of the remaining five isolates, three had MICs of 3 mg/L which is considered susceptible by EUCAST guidelines but non-susceptible by CLSI guidelines, and two isolates were unavailable for confirmation.

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 226 (47.0%) were phenotypically vancomycin non-susceptible (MIC >4 mg/L). One hundred and ten (22.9%) and 120 (24.9%) isolates were teicoplanin non-susceptible by CLSI and EUCAST guidelines respectively. Fourteen (2.9%) isolates were initially reported as linezolid non-susceptible (CLSI breakpoint >2 mg/L). However by Etest® nine of the 14 isolates had a linezolid MICs of ≤2 mg/L and therefore were considered susceptible. Of the remaining five isolates, three had MICs of 3 mg/L which is considered susceptible by EUCAST guidelines but non-susceptible by CLSI guidelines, and two isolates were unavailable for confirmation.

Genotypic Vancomycin Susceptibility Results

vanA/vanB PCR results were available for 328 of the 602 E. faecalis isolates. Two of the 328 isolates harbour a vanB gene. Both isolates had a vancomycin MIC of 8.0 mg/L.

The presence of vanA/B genes was determined by PCR or whole genome sequencing on 479 of the 481 E. faecium isolates. Overall 244 (50.9%) of the 479 isolates harbour a vanA and/or vanB gene. One hundred and thirteen of the vancomycin non-susceptible E. faecium isolates harboured vanA (Vitek® vancomycin MIC >4 mg/L). A further 110 E. faecium vancomycin non-susceptible isolates harboured vanB. Three isolates harboured vanA and vanB genes.
Table 1: The number and proportion of *E. faecalis* non-susceptible to ampicillin and the non-β-lactam antimicrobials, Australia, 2017

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Tested</th>
<th>Breakpoint (mg/L)</th>
<th>Non-Susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>602</td>
<td>&gt;8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>601</td>
<td>&gt;4&lt;sup&gt;c&lt;/sup&gt;</td>
<td>2</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>572</td>
<td>&gt;0.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>508</td>
</tr>
<tr>
<td>Tetracycline/Doxycycline</td>
<td>565</td>
<td>&gt;4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>419</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>546</td>
<td>&gt;1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>67</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>580</td>
<td>&gt;4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2</td>
</tr>
<tr>
<td>Teicoplanin</td>
<td>601</td>
<td>&gt;8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0</td>
</tr>
<tr>
<td>Linezolid</td>
<td>601</td>
<td>&gt;2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>595</td>
<td>&gt;32&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;64&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1</td>
</tr>
<tr>
<td>High Level Gentamicin</td>
<td>591</td>
<td>&gt;128&lt;sup&gt;b&lt;/sup&gt;</td>
<td>123</td>
</tr>
</tbody>
</table>

<sup>a</sup> CLSI non-susceptible breakpoint  
<sup>b</sup> EUCAST non-susceptible breakpoint  
<sup>c</sup> CLSI and EUCAST non-susceptible breakpoint

Eighteen vancomycin-susceptible *E. faecium* isolates were found to harbour vanA or vanB genes. Seven isolates harboured vanA (Vitek® vancomycin MIC ≤ 0.5 mg/L [4 isolates], MIC = 1 mg/L [2 isolates], MIC = 2.0 mg/L [1 isolate], teicoplanin ≤1mg/L [7 isolates]). Eleven isolates harboured vanB (Vitek® vancomycin MIC = 1.5 mg/L).

**E. faecium** Molecular Epidemiology

Of the 481 episodes, 461 *E. faecium* isolates were available for typing by WGS. The 461 isolates were classified into 64 sequence types (STs) including nine STs with 10 or more isolates (Table 3). Of the 55 STs with <10 isolates, 47 had only one isolate. Overall 369 (80%) of the 461 isolates were grouped into the nine major STs. Using eBURST, all nine major STs were grouped into CC17.

Geographical distribution of the STs varied (Table 3). For the nine major STs, ST17 (72 isolates) was identified in all regions except the Australian Capital Territory, the Northern Territory and Tasmania; ST1421 (70 isolates) was identified in all regions except the Northern Territory and Western Australia; ST796 (63 isolates) in all regions except the Australian Capital Territory, the Northern Territory and Western Australia; ST1424 (62 isolates) in all regions except the Northern Territory, South Australia, Tasmania and Western Australia; ST80 (42 isolates) found in all regions except the Northern Territory; ST555 (21 isolates) found in all regions...
Table 2: The number and proportion of *E. faecium* non-susceptible to ampicillin and the non-β-lactam antimicrobials, Australia, 2017

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Tested</th>
<th>Breakpoint (mg/L)</th>
<th>Non-Susceptible n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ampicillin</strong></td>
<td>481</td>
<td>&gt;8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>431</td>
<td>89.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>432</td>
<td>89.8</td>
</tr>
<tr>
<td><strong>Vancomycin</strong></td>
<td>481</td>
<td>&gt;4&lt;sup&gt;c&lt;/sup&gt;</td>
<td>226</td>
<td>47.0</td>
</tr>
<tr>
<td><strong>Erythromycin</strong></td>
<td>466</td>
<td>&gt;0.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>437</td>
<td>93.8</td>
</tr>
<tr>
<td><strong>Tetracycline/Doxycycline</strong></td>
<td>461</td>
<td>&gt;4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>285</td>
<td>61.8</td>
</tr>
<tr>
<td><strong>Ciprofloxacin</strong></td>
<td>444</td>
<td>&gt;1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>410</td>
<td>92.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>390</td>
<td>87.8</td>
</tr>
<tr>
<td><strong>Teicoplanin</strong></td>
<td>481</td>
<td>&gt;8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>110</td>
<td>22.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>120</td>
<td>24.9</td>
</tr>
<tr>
<td><strong>Linezolid</strong></td>
<td>481</td>
<td>&gt;2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Nitrofurantoin</strong></td>
<td>471</td>
<td>&gt;32&lt;sup&gt;a&lt;/sup&gt;</td>
<td>367</td>
<td>77.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;64&lt;sup&gt;b&lt;/sup&gt;</td>
<td>250</td>
<td>53.1</td>
</tr>
<tr>
<td><strong>High Level Gentamicin</strong></td>
<td>473</td>
<td>&gt;128&lt;sup&gt;a&lt;/sup&gt;</td>
<td>228</td>
<td>48.2</td>
</tr>
</tbody>
</table>

<sup>a</sup> CLSI non-susceptible breakpoint
<sup>b</sup> EUCAST non-susceptible breakpoint
<sup>c</sup> CLSI and EUCAST non-susceptible breakpoint

except the Australian Capital Territory, New South Wales and Queensland; ST203 (14 isolates) found in all regions except the Australian Capital Territory, the Northern Territory and Western Australia; ST18 (14 isolates) found in all regions except the Northern Territory, South Australia and Tasmania; and ST78 (11 isolates) identified only in New South Wales and Queensland.

ST1421 was the second most predominant ST in AESOP 2017 and was first described in AESOP 2015. In AESOP 2016 there were three single locus variants (slvs) of ST1421, classified as ST1422, ST1423 and ST1424. A fourth slv, named M-type 5, was identified in AESOP 2017. In all five STs the MLST *pstS* housekeeping gene was absent.

*vanA* was detected in five major STs (104 isolates, ST1421, ST17, ST1424, ST80 and ST203). *vanB* was detected in eight major STs (111 isolates, ST17, ST796, ST1424, ST80, ST555, ST203, ST18 and ST78) (Table 4). One ST796 isolate harboured *vanA* and *vanB* genes. Seven minor STs (eight isolates) harboured *vanB* genes, four minor STs (one isolate) harboured *vanA* genes and one minor ST (one isolate) harboured *vanA* and *vanB* genes.

**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
<table>
<thead>
<tr>
<th>ST</th>
<th>ACT</th>
<th>NSW</th>
<th>NT</th>
<th>Qld</th>
<th>SA</th>
<th>Tas</th>
<th>Vic</th>
<th>WA</th>
<th>Aus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>ST17</td>
<td>6</td>
<td>3.8</td>
<td>20</td>
<td>45.5</td>
<td>1</td>
<td>3.8</td>
<td>13</td>
<td>10.0</td>
<td>32</td>
</tr>
<tr>
<td>ST1421</td>
<td>9</td>
<td>42.9</td>
<td>41</td>
<td>25.9</td>
<td>1</td>
<td>2.3</td>
<td>2</td>
<td>7.7</td>
<td>1</td>
</tr>
<tr>
<td>ST796</td>
<td>4</td>
<td>2.5</td>
<td>1</td>
<td>25.0</td>
<td>1</td>
<td>2.3</td>
<td>1</td>
<td>3.8</td>
<td>4</td>
</tr>
<tr>
<td>ST1424</td>
<td>3</td>
<td>14.3</td>
<td>57</td>
<td>36.1</td>
<td>1</td>
<td>2.3</td>
<td>1</td>
<td>0.8</td>
<td>62</td>
</tr>
<tr>
<td>ST80</td>
<td>4</td>
<td>19.0</td>
<td>7</td>
<td>44</td>
<td>4</td>
<td>9.1</td>
<td>1</td>
<td>3.8</td>
<td>1</td>
</tr>
<tr>
<td>ST555</td>
<td>4</td>
<td>19.0</td>
<td>2</td>
<td>50.0</td>
<td>1</td>
<td>2.3</td>
<td>8</td>
<td>30.8</td>
<td>1</td>
</tr>
<tr>
<td>ST18</td>
<td>4</td>
<td>19.0</td>
<td>1</td>
<td>0.6</td>
<td>3</td>
<td>6.8</td>
<td>4</td>
<td>3.1</td>
<td>2</td>
</tr>
<tr>
<td>ST203</td>
<td>4</td>
<td>2.5</td>
<td>3</td>
<td>6.8</td>
<td>1</td>
<td>3.8</td>
<td>2</td>
<td>11.8</td>
<td>4</td>
</tr>
<tr>
<td>ST78</td>
<td>8</td>
<td>5.1</td>
<td>3</td>
<td>6.8</td>
<td>11</td>
<td>2.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>4.8</td>
<td>30</td>
<td>19.0</td>
<td>1</td>
<td>25.0</td>
<td>12</td>
<td>27.9</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>100</td>
<td>158</td>
<td>100</td>
<td>4</td>
<td>100</td>
<td>44</td>
<td>100</td>
<td>26</td>
</tr>
</tbody>
</table>

ACT = Australian Capital Territory; NSW = New South Wales; NT = Northern Territory; Qld = Queensland; SA = South Australia; Tas = Tasmania; Vic = Victoria; WA = Western Australia; Aus = Australia
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, comparison of Australian antimicrobial resistance data with other countries is possible.13

In the 2017 European Centre for Disease Prevention and Control (ECDC) enterococci surveillance program, the European Union/European Economic Area (EU/EEA) population-weighted mean percentage of *E. faecium* resistant to vancomycin was 14.9% (95% CI, 14–16), which represents a significant increase from 2014 when the percentage was 10.4%. The national percentages ranged from 0.0% in Iceland (95% CI, 0–20), Luxembourg (95% CI, 0–10), Malta (95% CI, 0–25) and Sweden (95% CI, 0–1) to 43.9% (95% CI, 28–60) in Cyprus.13

In AESOP 2017, approximately 42.3% of enterococcal bacteraemia were due to *E. faecium*, of which 47.0% (95% CI, 42.5–51.6) were phenotypically vancomycin non-susceptible by Vitek® or Phoenix™. However 50.9% of *E. faecium* isolates tested (244/479) harboured *vanA/vanB* genes, of which 47.0% (95% CI, 42.5–51.6) were phenotypically vancomycin non-susceptible by Vitek2® or Phoenix. Consequently, 25.1% (120/479) of *E. faecium* isolates harboured a *vanA* gene. There has been a significant increase in *vanA* *E. faecium* in Australia over the last four AGAR surveys from 6% (8/310) in AESOP 2013,14 9.5% (35/370) in 2014,15 20.7% (82/397) in 201516 and 21.6% (88/408) in 2016.17 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, 2013, 2014, 2015 and 2016, 37.0%, 48.6%, 51.1%, 49.3% and 50.9% of *E. faecium* respectively harboured *vanA/vanB*, confirming the incidence of vancomycin-resistant *E. faecium* bacteraemia in Australia is a significant problem.

Eleven (9.1%) of the 121 *vanB* *E. faecium* and seven (5.8%) of the 120 *vanA* *E. faecium* isolates had a vancomycin MIC at or below the CLSI and EUCAST susceptible breakpoint (≤4 mg/L) and therefore would not have been identified using routine phenotypic antimicrobial susceptibility methods.

By WGS, *E. faecium* was shown to be very polyclonal, consistent with the known plasticity of the enterococcal genome. The nine major *E. faecium* STs form 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 2017, nine *E. faecium* STs predominated: ST1421 (of which 84.3% of isolates harboured *vanA* genes); ST17 (13.8% *vanB*, 1.5% *vanA*); ST796 (93.5% *vanB*, 1.6% *vanA* and *vanB*); ST 1424 (54.8% *vanA*, 1.6% *vanB*); ST80 (21.4% *vanA*, 23.8% *vanB*); ST555 (73.7% *vanB*); ST203 (35.7% *vanB*, 7.1% *vanA*); ST18 (33.3% *vanB*) and ST78 (100% *vanB*).

Conclusions

The AESOP 2017 study has shown that, although predominately caused by *E. faecalis*, enterococcal bacteraemia in Australia is frequently caused by ampicillin-resistant, high-level gentamicin-resistant vancomycin-resistant *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 a predominant genotype, the number of *vanA* *E. faecium* isolates identified in AESOP 2017 has significantly increased when compared to AESOP 2013–2016. 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. Ongoing studies on the enterococcal genome will contribute to our understanding of the rapid and ongoing
Table 4: The number and proportion of major *Enterococcus faecium* sequence types harbouring *vanA/B* genes, Australia, 2017

<table>
<thead>
<tr>
<th>ST</th>
<th>n</th>
<th>vanA</th>
<th></th>
<th></th>
<th>vanB</th>
<th></th>
<th></th>
<th>vanA and vanB</th>
<th></th>
<th></th>
<th>Not Detected</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST17</td>
<td>72</td>
<td>1</td>
<td>1.4</td>
<td></td>
<td>9</td>
<td>12.5</td>
<td></td>
<td>62</td>
<td>86.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST1421</td>
<td>70</td>
<td>59</td>
<td>84.3</td>
<td></td>
<td>11</td>
<td>15.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST796</td>
<td>63</td>
<td>59</td>
<td>93.7</td>
<td>1</td>
<td>1.6</td>
<td></td>
<td>3</td>
<td>4.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST1424</td>
<td>62</td>
<td>34</td>
<td>54.8</td>
<td>1</td>
<td>1.6</td>
<td></td>
<td>27</td>
<td>43.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST80</td>
<td>42</td>
<td>9</td>
<td>21.4</td>
<td>10</td>
<td>23.8</td>
<td></td>
<td>23</td>
<td>54.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST555</td>
<td>21</td>
<td>16</td>
<td>76.2</td>
<td></td>
<td>5</td>
<td>23.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST18</td>
<td>14</td>
<td>4</td>
<td>28.6</td>
<td></td>
<td>10</td>
<td>71.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST203</td>
<td>14</td>
<td>1</td>
<td>7.1</td>
<td>5</td>
<td>35.7</td>
<td>8</td>
<td>57.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST78</td>
<td>11</td>
<td>11</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>92</td>
<td>8</td>
<td>8.7</td>
<td>4</td>
<td>4.3</td>
<td>1</td>
<td>1.1</td>
<td>79</td>
<td>85.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>461</td>
<td>112</td>
<td>24.3</td>
<td>119</td>
<td>25.8</td>
<td>2</td>
<td>0.4</td>
<td>228</td>
<td>49.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The evolution of enterococci in the hospital environment and assist in preventing their nosocomial transmission.

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital
Sebastiaan van Hal and Alicia Beukers, Royal Prince Alfred Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital
James McLeod, Alice Springs Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Northern Territory**

Rob Baird and Jann Hennessy, Royal Darwin Hospital

**Western Australia**

Jock Harkness and David Lorenz, St Vincent’s Hospital

**South Australia**

South Australian Health and Medical Research Institute

**Tasmania**

Peter Huntington, Royal North Shore Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Northern Territory**

Rob Baird and Jann Hennessy, Royal Darwin Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.

**Members of the AGAR in 2017 were:**

**Australian Capital Territory**

Peter Collignon and Susan Bradbury, The Canberra Hospital

**New South Wales**

Thomas Gottlieb and Graham Robertson, Concord Hospital

**Queensland**

Enzo Binotto and Bronwyn Thomsett, Pathology Queensland Cairns Base Hospital

**Acknowledgments**

This study was funded by a grant from the Australian Commission on Safety and Quality in Healthcare.
Graeme Nimmo and Narelle George, Pathology Queensland Central Laboratory, Royal Brisbane and Women’s Hospital

Petra Derrington and Cheryl Curtis, Pathology Queensland Gold Coast Hospital

Robert Horvath and Laura Martin, Pathology Queensland Prince Charles Hospital

Naomi Runnegar and Joel Douglas, Pathology Queensland Princess Alexandra Hospital

Jennifer Robson and Georgia Peachey, Sullivan Nicolaides Pathology, Greenslopes Hospital

Clare Nourse, Lady Cilento Children’s Hospital

South Australia

Kelly Papanaoum and Xiao Ming Chen, SA Pathology (Flinders Medical Centre)

Morgyn Warner and Kija Smith, SA Pathology (Royal Adelaide Hospital and Women’s and Children’s Hospital)

Tasmania

Louise Cooley and David Jones, Royal Hobart Hospital

Pankaja Kalukottege and Kathy Wilcox, Launceston General Hospital

Victoria

Denis Spelman and Rose Bernhard, The Alfred Hospital

Paul Johnson and Frances Hurren, Austin Health

Tony Korman and Despina Kotsanas, Monash Medical Centre and Monash Children’s Hospital

Andrew Daley and Gena Gonis, Royal Women’s and Children’s Hospital

Mary Jo Waters and Lisa Brenton, St Vincent’s Hospital

Western Australia

David McGechie and Denise Daley, PathWest Laboratory Medicine – WA Fiona Stanley Hospital

Ronan Murray and Jacinta Bowman, PathWest Laboratory Medicine – WA Sir Charles Gairdner Hospital

Michael Leung and Jacinta Bowman, PathWest Laboratory Medicine – Northwest WA

South Australia

Owen Robinson and Geoffrey Coombs, PathWest Laboratory Medicine – WA Royal Perth Hospital

Tasmania

Sudha Pottumarthy-Boddu and Fay Kappler, Australian Clinical Laboratories, St John of God Hospital, Murdoch

Shalinie Perera and Ian Meyer, Western Diagnostic Pathology, Joondalup Hospital

Victoria

Christopher Blyth, Princess Margaret Hospital for Children

Author details

Prof Geoffrey W Coombs¹,², Ms Denise A Daley³, Ms Yung Thin Lee⁴, Dr Stanley Pang¹,², on behalf of the Australian Group on Antimicrobial Resistance

1. Antimicrobial Resistance and Infectious Disease (AMRID) Research Laboratory, Murdoch University, Murdoch, Western Australia, Australia

2. Department of Microbiology, PathWest Laboratory Medicine-WA, Fiona Stanley Hospital, Murdoch, Western Australia, Australia

3. Australian Group on Antimicrobial Resistance, Fiona Stanley Hospital, Murdoch, Western Australia, Australia
Corresponding Author

Prof Geoffrey Coombs

Antimicrobial Resistance and Infectious Disease (AMRID) Research Laboratory, Murdoch University, Murdoch, Western Australia, Australia

Telephone: +61 8 6152 2397

Email: g.coombs@murdoch.edu.au

References


