

## Peer-reviewed articles

# CHANGING EPIDEMIOLOGY OF BLOODSTREAM INFECTION PATHOGENS OVER TIME IN ADULT NON-SPECIALTY PATIENTS AT AN AUSTRALIAN TERTIARY HOSPITAL

Ar Kar Aung, Matthew J Skinner, Felicity J Lee, Allen C Cheng

## Abstract

The epidemiology of bloodstream infections (BSI) has been changing over time in developed countries. However, overview reports of BSI trends are limited in Australia. This descriptive epidemiological study analysed general and age-group specific trends, and antimicrobial susceptibility patterns of blood culture isolates between 2001 and 2009 in non-specialty adult patients at an Australian tertiary referral centre. A total of 3,051 isolates from 2,172 patients (60% males) were analysed. Both community onset (1,790 isolates, 59%) and hospital onset (1,261 isolates, 41%) BSIs were included. The mean age of patients was  $59 \pm 20$  years; 930 patients (43%) were 70 years of age or over. Overall, 1,493 (49%) gram positive bacteria, 1,389 (46%) gram negative bacteria and 169 (5.5%) fungi were isolated. The proportion of gram negative isolates increased over the 9 years, (44% to 53%,  $P=0.006$ ) whilst gram positives decreased (49% to 45%,  $P=0.045$ ). These trends were significant in community onset infections but not hospital onset infections, and also in adult patients ( $\geq 20$  to  $<70$  years) but not in the elderly ( $\geq 70$  years). Gram negative pathogens were most prevalent amongst the elderly (53% in the  $\geq 70$  years age group,  $P<0.0001$  vs 41% in the  $\geq 20$  to  $<70$  years age group), attributable to an age-dependent increase in *Escherichia coli* infections and a decrease in *Staphylococcus aureus* infections ( $P<0.0001$  for both). Most gram negative isolates remained susceptible to commonly prescribed antibiotics. By contrast, methicillin-resistant *S. aureus* rates decreased from 54% in 2001 to 28% in 2009 ( $P=0.007$ ). This study found that gram negative BSIs appeared to be re-emerging, particularly in community onset infections and also amongst the younger patients at the study institution. Such epidemiological trends have important implications for antimicrobial choices for the treatment of undifferentiated sepsis. *Commun Dis Intell* 2012;36(4):E333–E341.

Keywords: bloodstream infections, gram positive organisms, gram negative organisms, epidemiology, antimicrobial susceptibility

## Introduction

Bloodstream infections (BSIs) are a major cause of morbidity and mortality worldwide. They contribute significantly to the healthcare burden and their management remains a constant challenge for physicians.<sup>1,2</sup> The epidemiology of BSIs is continually changing. Since the early 1980s there has been a gradual shift towards gram positive organisms being the predominant pathogens for BSIs in developed countries, in both community and healthcare-associated settings.<sup>2,3</sup> By contrast, gram negative organisms remain the more prevalent BSI pathogens in developing countries.<sup>4,5</sup> However, there has been a recent re-emergence of gram negative organisms, particularly in developed countries, contributing up to 55% of community-associated BSIs.<sup>6–9</sup> The prevalence of gram negative infections is also known to increase with age, and elderly patients are most vulnerable to high morbidity and mortality from these BSIs.<sup>1,10–13</sup>

Among the BSI pathogens in developed countries, *Staphylococcus aureus* is the most frequently isolated gram positive pathogen, whilst *Escherichia coli* is the most frequently isolated gram negative pathogen.<sup>6,7,10,14,15</sup> The antimicrobial susceptibility patterns of common BSI isolates have also been changing over time.<sup>3,14,16,17</sup> A concerning increase in infections with methicillin-resistant *S. aureus* (MRSA) worldwide as well as resistant gram negative isolates to commonly used antimicrobials has been described.<sup>17,18</sup>

Despite regular reporting of epidemiologic data in other developed parts of the world, such overview reports on BSI trends are limited in Australia.<sup>19,20</sup> Moreover, current Therapeutic Guidelines recommend the use of intravenous flucloxacillin and gentamicin as empiric treatment for all patients presenting with undifferentiated sepsis.<sup>21</sup> However, recent epidemiological studies to support or refute these recommendations are lacking. In addition, these recommendations do not take into account the age-specific distribution of BSI organisms and that elderly patients are more prone to unwanted side effects of

antibiotic treatment. All these factors pose significant challenges for the management of undifferentiated sepsis for the hospital inpatient population, which comprises both community and hospital onset infections. This descriptive epidemiological study was conducted with the aim of reviewing the changing trends in the epidemiology of BSI pathogens, and the antimicrobial susceptibility patterns for the most commonly isolated organisms over a 9-year period, among non-specialty inpatients at a single Australian tertiary institution. The study further stratified the overall trends into community and hospital onset infections and two age groups: adults ( $\geq 20$  years to  $< 70$  years) and the elderly ( $> 70$  years) to determine any strata-specific trends.

## Methods

This study was conducted at The Alfred; a 380 bed adult tertiary referral centre and university teaching hospital, in Melbourne, Australia. Approval to conduct the study was obtained from the hospital ethics committee prior to commencement.

BSI isolates collected between 1 January 2001 and 31 December 2009 from patients aged 20 years or over were identified. Both community and hospital onset infections were included. Community onset infections were defined as the time from hospital admission to the first positive blood culture of 48 hours or less, and hospital onset infections as occurring more than 48 hours post-admission. Information on patient demographics, positive blood culture isolates and antimicrobial susceptibilities were extracted from computerised admission and routine laboratory databases.

## Study population

Organ transplant recipients, haematology, oncology, respiratory (including cystic fibrosis) and burns patients were excluded as they represented heterogenous populations. Patients included in the study were from 'non-specialty' populations, defined as any patient from an inpatient unit who did not meet the above exclusion criteria. They included all patients from general medicine, sub-specialty medicine units (including patients on haemodialysis), psychiatry, radiation oncology, general surgery and surgical specialties (including trauma but not the burns unit). These patients were chosen as they represented a more homogenous group who were not heavily immunocompromised nor were they likely to have bloodstream infections with distinct pathogens, thereby closely representing the general patient population.

Coagulase negative staphylococci isolates were excluded as it was not possible to retrospectively differentiate between true infection and contamina-

tion. Duplicate isolates, defined as the growth of the same organism within 14 days of the primary blood culture with the same antibiograms, were counted as a single BSI episode.

During the period of this study, *in vitro* antimicrobial susceptibility data for BSI isolates and minimum inhibitory concentration (MIC) breakpoints were reported by the laboratory in accordance with the British Society of Antimicrobial Chemotherapy guidelines using the disc diffusion method.<sup>22</sup>

## Statistical analysis

All statistical analyses were performed using GraphPad Prism 4.0 (GraphPad Software, San Diego, CA). Continuous numerical data were expressed as mean  $\pm$  standard deviation and categorical data were expressed as count and proportions. Dichotomous age groups of adult and elderly were pre-defined for statistical analysis. These age groups were chosen to reflect the published epidemiology of BSIs and associated mortality in the elderly, and are also in accordance with recent studies of the elderly populations.<sup>23-25</sup>

Simple linear regression analyses were performed using years as independent variables and proportions of gram positive and gram negative organisms in a given year as dependent variables to detect significant trends over time. These trends were further stratified according to community and hospital onset BSIs and pre-defined age groups of adult and elderly to further detect category specific trends. Similar linear regression analyses were performed on antimicrobial susceptibility data, with per cent susceptibility as dependent variables, for key isolates to antimicrobials of interest. With all linear regression analyses, normality of distribution was assumed and a two sided *P*-value of less than 0.05 was considered significant, provided the coefficient of determination,  $R^2 \geq 0.3$ .

Pearson's chi-square tests were used to measure the differences in the proportions of gram positive and gram negative BSIs and the proportions of individual BSI organisms between the pre-defined age categories. In these analyses, the proportions over the 9-year period were collapsed into overall proportions in each age group. A two sided *P*-value of less than 0.05 was considered statistically significant for chi-square tests.

## Results

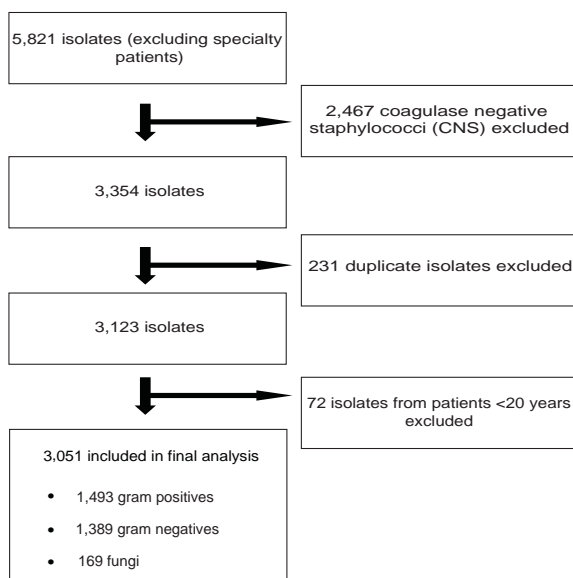
A total of 5,821 blood culture isolates were identified over a 9-year period. After exclusions (Figure 1), 3,051 isolates were included for further analysis. These isolates represented a total of 2,172 patients (60% males). Of the excluded blood cultures,

coagulase negative staphylococci were isolated from 2,467 samples (42% of all positive blood cultures). Other excluded samples were 72 from patients aged less than 20 years and 231 duplicates. The mean age of patients was  $59 \pm 20$  years and 930 (43%) patients were in the elderly age group.

Table 1 details BSI isolates over the 9-year period, with figures for the lead pathogen in each group. Overall, there were 1,493 (49%) gram positive isolates, 1,389 (46%) gram negative isolates and 169 (5.5%) fungal isolates. Of the isolates analysed, 1,790 (59%) were community onset whilst 1,261 (41%) were hospital onset BSIs. Community onset BSIs comprised 861 (48%) gram positive, 904 (51%) gram negative and 25 (1.4%) fungal isolates while hospital onset BSIs, comprised 632 (50%) gram positive, 485 (39%) gram negative and 144 (11%) fungal isolates.

A statistically significant increase in the proportion of gram negative pathogens was evident over time (44% in 2001 to 53% in 2009,  $P = 0.006$ ) with a concomitant decrease in the proportion of gram positive pathogens (49% in 2001 to 45% in 2009,  $P = 0.045$ ) (Figure 2). Community onset BSIs showed similar statistically significant trends in increasing proportions of gram negative pathogens and decreasing proportions of gram positive pathogens over time (Figure 3). By contrast, no statistically significant changes in trends over time were detected for hospital onset BSIs (Figure 4). When stratified according to age groups, statistically significant trends in increasing gram negative infections and decreasing gram positive infections were observed over time in the adult age group (Figure 5). However, these trends were not evident

**Figure 1: A flow diagram outlining the selection process for isolates**



**Table 1: Bloodstream infection isolates, 2001 to 2009, by organism**

Year	2001		2002		2003		2004		2005		2006		2007		2008		2009		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
<b>Gram positives</b>	189	48.7	250	61.0	216	51.3	175	47.9	145	44.3	142	48.0	137	45.5	127	43.2	112	45.0	1,493	48.9
<i>S. aureus</i>	100	25.8	138	33.7	107	25.4	87	23.8	78	23.9	72	24.3	57	18.9	47	16.0	45	18.1	731	24.0
<b>Gram negatives</b>	169	43.6	137	33.4	177	42.0	168	46.0	162	49.5	142	48.0	151	50.2	152	51.7	131	52.6	1,389	45.5
<i>E. coli</i>	55	14.2	54	13.2	70	16.6	63	17.3	73	22.3	81	27.4	80	26.6	74	25.2	68	27.3	618	20.3
<b>Fungi</b>	30	7.7	23	5.6	28	6.7	22	6.0	20	6.1	12	4.1	13	4.3	15	5.1	6	2.4	169	5.5
<i>C. albicans</i>	13	3.4	13	3.2	13	3.1	12	3.3	10	3.1	6	2.0	8	2.7	9	3.1	2	0.8	86	2.8
<b>Total BSI episodes</b>	388	100.0	410	100.0	421	100.0	365	100.0	327	100.0	296	100.0	301	100.0	294	100.0	249	100.0	3,051	100.0

BSI Bloodstream infections.

in the elderly age group (Figure 6). Results of linear regression analyses were further summarised in Table 2.

*S. aureus* (731 isolates, 24%) remained the most common BSI pathogen followed by *E. coli* (618 isolates, 20%); *Klebsiella pneumoniae* (160 isolates, 5.2%); *Enterococcus faecalis* (156 isolates, 5.1%) and *Pseudomonas aeruginosa* (112 isolates, 3.7%). The proportion of fungal BSIs was low (169 isolates, 5.5%), with *Candida albicans* being most frequently isolated (86 isolates, 2.8%).

Gram negative BSIs were significantly more common in the elderly patients (41% in the adult age group vs 53% in the elderly age group,  $P < 0.0001$ ) whilst gram positive infections were more common in the younger patients (54% in the adult age group vs 42% in the elderly age group,  $P < 0.0001$ ). This finding was mainly mediated by an increase in prevalence of *E. coli* BSIs (15% in the adult age group vs 28% in the elderly age group,  $P < 0.0001$ ) with a concurrent decrease in prevalence of *S. aureus* BSIs with age (27% in the adult age group vs 19% in the elderly age group,  $P < 0.0001$ ). No other statistically significant age group specific differences in proportions were observed for other pathogens in the top rank order.

In terms of antimicrobial sensitivity (Table 3), the percentage of methicillin-resistant *S. aureus* (MRSA) BSI episodes decreased from 54% in 2001 to 28% in 2009 ( $P = 0.007$ ). Most *Ent. faecalis* isolates remained susceptible to amoxicillin, and this trend did not change over time ( $P = 0.13$ ); although an increase in vancomycin resistance was noted over this 9-year period ( $P = 0.035$ ). A similar trend in vancomycin resistance was also observed for *Ent. faecium* isolates ( $P = 0.012$ ); however, their overall numbers remained relatively small.

Most *E. coli* isolates remained susceptible to gentamicin and carbapenems but an increase in resistance to third-generation cephalosporins and ciprofloxacin was observed ( $P = 0.027$  and  $0.019$  respectively). There was a significant increase in ceftazidime resistance in *E. coli* ( $P = 0.013$ ), indicating an increase in the number of extended spectrum beta-lactamase inhibitor producing organisms, but the overall proportions remained low (<5%). Other key gram negative isolates remained susceptible to the commonly used antibiotics. Interestingly, gentamicin resistance decreased over time in *Klebsiella spp.* ( $P = 0.044$ ) (Table 1).

## Discussion

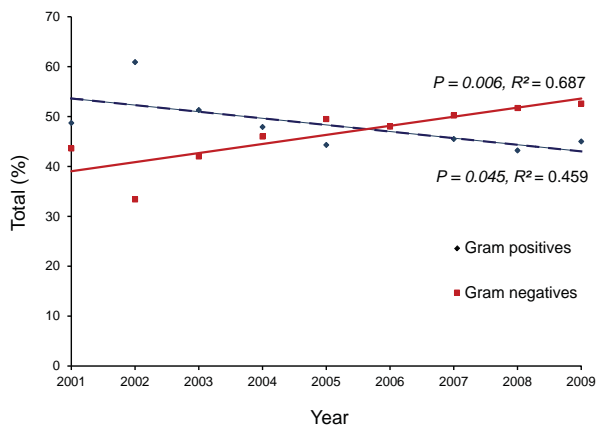
In certain developed regions of the world, such as North America and Europe, the epidemiological data on BSI pathogens and their antimicrobial

susceptibilities have been published at regular intervals.<sup>14,16,17</sup> Likewise, in the Australasian region, the Australian Group on Antimicrobial Resistance has taken the lead in reporting the epidemiology of specific BSI pathogens such as *S. aureus*.<sup>26–28</sup> Although state-based surveillance programs are in place throughout Australia to monitor the epidemiology of bloodstream infections, reports from such programs are limited.<sup>29</sup> This study is one of the few Australian studies that has analysed trends for a range of pathogens to describe trends in the epidemiology of BSIs at a single referral centre.<sup>19,20,30,31</sup> One aim of this study was to encourage other Australian tertiary institutions to report epidemiological data of a similar nature, thus allowing for the collation of more generalisable regional and national data on the epidemiology of BSIs.

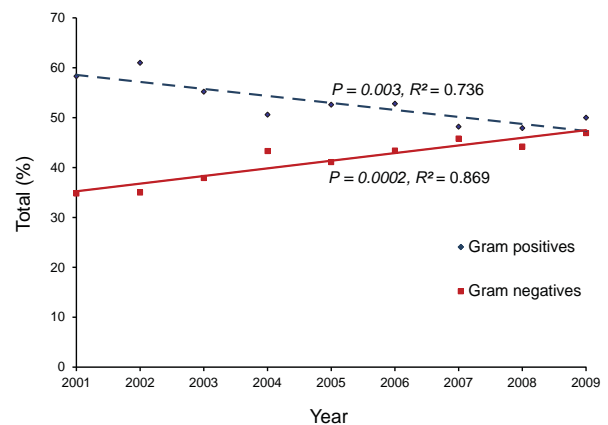
At the study institution, gram positive BSIs remained prevalent overall in the non-specialty patient population over the last 9 years. However, there was a significant increase in the prevalence of gram negative BSIs with a concomitant decrease in gram positive BSIs over time. This trend appears to have been mediated by the changing epidemiology in community onset but not hospital onset infections and, also in the younger adult age group. Gram negative pathogens remained the predominant cause of BSI in the elderly. Whilst *E. coli* resistance to third-generation cephalosporins and ciprofloxacin increased over time, antimicrobial susceptibilities for other gram negative organisms remained relatively stable. Vancomycin-resistant enterococci (VRE) infection rates had increased but MRSA rates had decreased.

In the last decade, gram negative pathogens have re-emerged as dominant contributors of BSIs in some developed countries, both in the healthcare-associated and community-acquired settings.<sup>6,7</sup> The study results appear to be consistent with these trends, although the trends for hospital onset BSIs failed to reach statistical significance. The reasons for this are unclear. However a change in the hospital patient population, local antimicrobial prescribing preferences and differing methods of clinical practice may play important roles.<sup>7</sup> Another possible contributing factor to this trend is the ageing population in developed countries, since gram negative infections are more common in the elderly and nursing home residents.<sup>11,13</sup> The study results challenged such assumptions. It was surprising to find that the changing epidemiology at the study institution was not mediated by the elderly age group, but rather by the adult age group. As with previous studies, it was found that in the elderly age group the likelihood of gram negative infections increased significantly. This demonstrates that there is a gradual shift towards infections involving enteric organisms with increasing age.

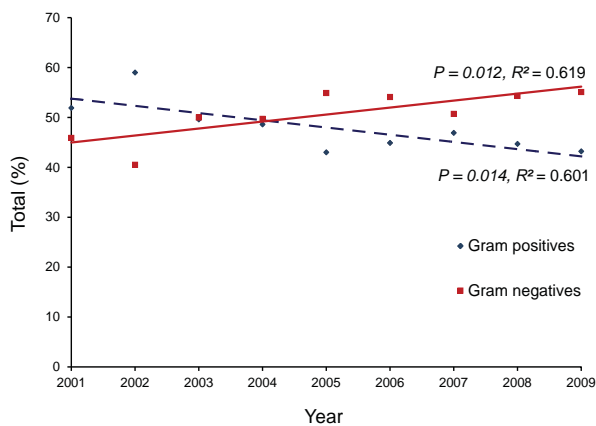
**Figure 2: The proportion of gram positive and gram negative pathogens, 2001 to 2009**



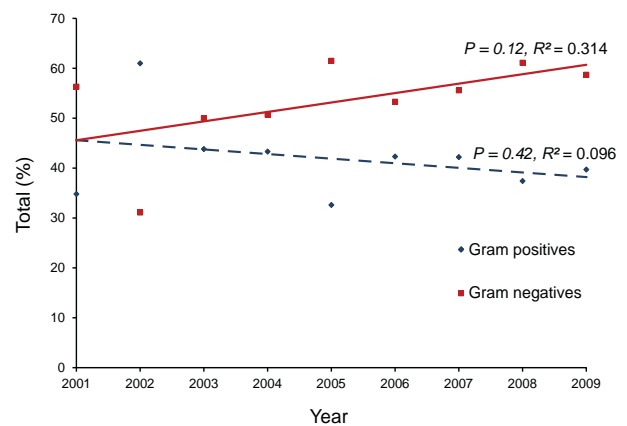
**Figure 5: The proportion of gram positive and gram negative pathogens in the  $\geq 20$  < 70 years age group, 2001 to 2009**



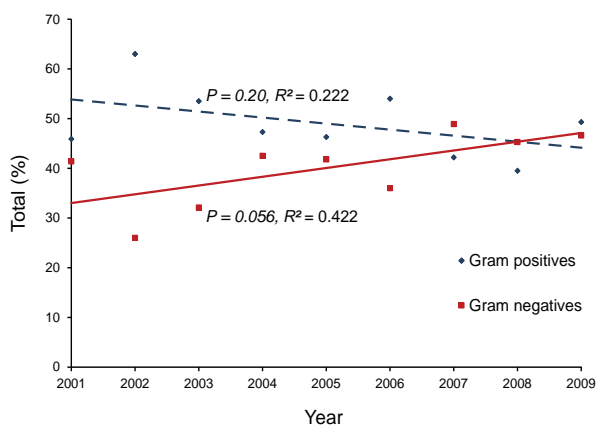
**Figure 3: The proportion of gram positive and gram negative pathogens in community onset bloodstream infections, 2001 to 2009**



**Figure 6: The proportion of gram positive and gram negative pathogens in the  $\geq 70$  years age group, 2001 to 2009**



**Figure 4: The proportion of gram positive and gram negative pathogens in hospital onset bloodstream infections, 2001 to 2009**



**Table 2: Linear regression analyses for proportions of gram positive and gram negative organisms**

Dependent variables	Gradient estimate	Intercept estimate	P-value	R <sup>2</sup>
<b>Figure 2 (overall)</b>				
Gram positives	-1.32	2,701.6	0.045	0.459
Gram negatives	1.82	-3,606.1	0.006	0.688
<b>Figure 3 (community onset)</b>				
Gram positives	-1.45	2,948.5	0.014	0.601
Gram negatives	1.40	-2,756.4	0.012	0.619
<b>Figure 4 (hospital onset)</b>				
Gram positives	-1.20	2,481.7	0.20	0.222
Gram negatives	1.76	-3,495.4	0.056	0.427
<b>Figure 5 (age <math>\geq 20</math> &lt; 70 years)</b>				
Gram positives	-1.41	2,870.0	0.003	0.736
Gram negatives	1.53	-3,029.6	0.0002	0.869
<b>Figure 6 (age <math>\geq 70</math> years)</b>				
Gram positives	-0.92	1,893.2	0.42	0.096
Gram negatives	1.89	-3,736.3	0.12	0.314

Independent variable = Years (2001 – 2009)

Table 3: Antimicrobial sensitivity for selected bloodstream pathogens, 2001 to 2009 (Number susceptible/Total, % susceptible)

Organisms and antimicrobials tested	2001		2002		2003		2004		2005		2006		2007		2008		2009		Total	
	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%
<b><i>Staphylococcus aureus</i></b>																				
Flucloxacillin	46/100	46.0	61/138	44.2	65/105	61.9	48/84	57.1	35/74	47.3	41/72	56.9	42/55	76.3	33/40	82.5	29/40	72.5	400/708	56.5
Erythromycin* (for MRSA only)	4/54	7.4	2/77	2.6	0/40	0.0	2/36	5.6	4/39	10.3	4/31	12.9	1/13	7.7	2/7	28.6	2/11	18.2	21/308	6.8
<b><i>Enterococcus faecalis</i></b>																				
Vancomycin	11/11	100.0	30/30	100.0	23/23	100.0	20/20	100.0	11/11	100.0	10/10	100.0	11/11	100.0	6/7	85.7	14/16	87.5	136/139	97.8
Amoxicillin	10/11	90.9	29/29	100.0	23/23	100.0	22/22	100.0	13/13	100.0	13/13	100.0	16/16	100.0	10/10	100.0	15/15	100.0	151/152	99.3
<b><i>Enterococcus faecium</i></b>																				
Vancomycin	3/3	100.0	7/8	87.5	6/7	85.7	5/6	83.3	4/6	66.7	4/5	80.0	7/10	70.0	7/9	77.8	1/4	25.0	44/58	75.9
Amoxicillin	2/3	66.7	2.8	25.0	3/7	42.9	1/6	16.7	1/6	16.7	0/5	0/0	2/10	20.0	0/10	0.0	0/4	0.0	11/59	18.6
<b><i>Escherichia coli</i></b>																				
Gentamicin	54/54	100.0	51/54	94.4	68/69	98.6	61/63	96.8	70/70	100.0	77/81	95.1	75/77	97.4	69/73	94.5	55/60	91.7	580/601	96.5
Third generation cephalosporin†	53/54	98.1	54/54	100.0	69/70	98.6	63/63	100.0	69/71	97.2	79/81	97.5	73/77	94.8	69/74	93.2	60/62	96.8	589/606	97.2
Ceftazidime‡	53/54	98.1	54/54	100.0	67/69	97.1	62/62	100.0	69/71	97.2	79/81	97.5	73/77	94.8	68/73	93.2	58/61	95.1	583/602	96.8
Meropenem	54/54	100.0	53/54	98.1	68/69	98.6	63/63	100.0	71/71	100.0	80/81	98.8	76/77	98.7	73/73	100.0	61/61	100.0§	599/603	99.3
Ciprofloxacin	54/54	100.0	51/54	94.4	67/69	97.1	61/63	96.8	67/71	94.4	79/81	97.5	72/77	93.5	68/73	93.2	56/61	91.8	576/603	95.4
<b><i>Klebsiella spp.</i></b>																				
Gentamicin	39/41	95.1	22/25	88.0	18/20	90.0	25/29	86.2	16/16	100.0	16/17	94.1	21/21	100.0	20/20	100.0	19/19	100.0	196/208	94.2
Third generation cephalosporin†	38/41	92.7	23/25	92.0	20/20	100.0	26/29	89.7	16/16	100.0	14/17	82.4	22/22	100.0	19/20	95.0	19/19	100.0	197/209	94.3
Ceftazidime‡	38/41	92.7	22/25	88.0	18/20	90.0	26/29	89.7	16/16	100.0	14/17	82.4	21/21	100.0	19/20	95.0	19/19	100.0	193/208	92.8
Meropenem	41/41	100.0	25/25	100.0	20/20	100.0	28/29	96.6	16/16	100.0	17/17	100.0	21/21	100.0	20/20	100.0	19/19	100.0	207/208	99.5
Ciprofloxacin	41/41	100.0	22/25	88.0	20/20	100.0	29/29	100.0	16/16	100.0	16/17	94.1	19/21	90.5	20/20	100.0	18/19	94.7	201/208	96.6
<b><i>Pseudomonas spp.</i></b>																				
Ciprofloxacin	11/11	100.0	11/12	91.7	16/18	88.9	11/15	73.3	13/18	72.2	10/11	90.9	8/8	100.0	11/11	100.0	5/6	83.3	96/110	87.3
Tobramycin	12/12	100.0	10/12	83.3	18/18	100.0	11/15	73.3	16/18	88.9	11/11	100.0	7/8	87.5	11/11	100.0	6/6	100.0	102/111	91.9
Meropenem	10/10	100.0	7/8	87.5	16/18	88.9	10/15	66.7	16/18	88.9	10/11	90.9	8/8	100.0	9/11	81.8	4/6	66.7	90/105	85.7

\* Erythromycin sensitivity was used as a surrogate marker for community-associated methicillin-resistant *Staphylococcus aureus* infections.

† Third generation cephalosporin susceptibility was determined by sensitivity to ceftiaxone or cefotaxime.

‡ Ceftazidime susceptibility was used as a surrogate marker for determination of extended spectrum beta-lactamase inhibitor production.

§ Susceptibility data based on 61 out of 68 isolates. Data was not known for 7 isolates.

N = total number of isolates tested, n = number of isolates susceptible.

Current Australian antibiotic guidelines recommend the use of intravenous flucloxacillin and gentamicin as empiric therapy for the treatment of undifferentiated sepsis regardless of a patient's age.<sup>21</sup> However, the appropriateness of this recommendation needs to be carefully considered in the elderly, who are more likely to have gram negative sepsis, and are more prone to the side effects of antimicrobial drugs. Although in principle, gentamicin would achieve broad cover for the gram negative pathogens, the use of aminoglycosides may be problematic in the elderly due to the risks of developing sensorineural hearing loss, vestibular toxicity and nephrotoxicity. These risks are known to increase with age-related hearing and renal impairment, concurrent ototoxic and nephrotoxic medication use, and the development of sepsis-associated multi-organ dysfunction. Hence, empiric treatment with alternative antimicrobial agents may be more suitable for elderly patients. Given the favourable susceptibility patterns of major gram negative isolates and decreasing MRSA rates in the study population, piperacillin/tazobactam or ticarcillin/clavulanate may be more appropriate first-line antimicrobials for the treatment of undifferentiated sepsis, for both community and hospital-onset bacteraemia.

At the start of the study period, the MRSA rates at The Alfred were high (>50% of total *S. aureus* isolates for a particular year) but towards the end of the study period, they decreased to the national average of around 25%.<sup>32</sup> It was unclear why there were such high MRSA rates, but lack of structured infection control programs in the early years may have contributed. Recent Australian studies have shown that the implementation of basic infection control measures, such as reinforcement of hand-hygiene and antimicrobial stewardship, significantly contributed to an overall decline in MRSA rates.<sup>33,34</sup> A subsequent decline in rates at this institution was likely attributable to the introduction of similar practices halfway through the study period. Further work is needed to elucidate causal relationships. It remains unclear as to why such infection control measures did not confer similar trends in VRE rates.

## Limitations

This study was conducted at a single institution and the results may not be generalisable to the whole Australian population. In addition, a selection bias may have occurred in excluding certain specialty patient populations such as solid organ and haematological transplant patients, oncology, cystic fibrosis and burns patients, thereby

resulting in a more homogenous general patient population with more favourable antimicrobial susceptibility profiles. Nonetheless, the main aim of this study was to evaluate the BSI trends in a general patient population who were not heavily immunosuppressed. Accordingly, this study has provided useful results and recommendations for the non-specialised patient population, which may be of some value to other tertiary centres. It is hoped that other centres will collate and publish their local data to provide further comparisons.

Secondly, in this study it was not possible to determine the exact number of hospital admissions and days of bed-separation per year in the study population, and therefore it was not possible to calculate the incident rates of BSIs.

Thirdly, although this study separated the BSI episodes into community onset and hospital onset infections according to time from admission to the first culture positivity ( $\leq 48$  hours vs  $> 48$  hours), without accompanying clinical data, misclassification could have occurred. Examples include those who had peripherally inserted central venous catheter associated infections or those who re-presented within 48 hours of discharge from a previous episode of care. This is an inherent limitation of a retrospective study. However, these results provided relatively close estimations of true community and hospital onset BSI episodes.

Lastly, due to the retrospective design, it was not possible to determine the relative contribution of coagulase negative staphylococci to the BSI epidemiology. Although this should be included in the analysis, BSIs with coagulase negative staphylococci are known to cause less significant mortality and morbidity when compared with other pathogens.<sup>7</sup>

## Conclusions

This study provides some insight into the local epidemiology of BSI pathogens. It was concluded that over the last decade, there has been a changing epidemiology of BSI pathogens at this institution with gram negative organisms becoming the key contributors. Community onset infections, particularly in younger patients, appeared to drive this trend. Exact contributing factors within these groups need to be further elucidated. Closer surveillance of these trends is needed at The Alfred, as well as nation-wide, for provision of appropriate antimicrobial therapy for undifferentiated sepsis.

## Author details

Dr Ar Kar Aung, Registrar in Infectious Diseases and General Medicine<sup>1,2</sup>

Dr Matthew J Skinner, General Medicine and Infectious Diseases Physician<sup>1,2</sup>

Dr Felicity J Lee, Resident Medical Officer<sup>1</sup>

A/Prof Allen C Cheng, Infectious Diseases and General Medicine Physician<sup>2,3</sup>

1. Department of Infectious Diseases and Microbiology, Sir Charles Gairdner Hospital, Nedlands, Western Australia
2. General Medical Unit, The Alfred, Prahran, Victoria
3. Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Victoria

Corresponding author: Dr Ar Kar Aung, General Medical Unit, The Alfred, Level 5, The Alfred Centre, Commercial Road, PRAHAN VIC 3181. Telephone: +61 3 9076 2000. Email: arkarau@yaho.com

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