# Infection management processes in intensive care and their association with mortality

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Received 5 October 2020; accepted 7 March 2021

**Background:** ICU-specific tables of antimicrobial susceptibility for key microbial species ('antibiograms'), antimicrobial stewardship (AMS) programmes and routine rounds by infectious diseases (ID) physicians are processes aimed at improving patient care. Their impact on patient-centred outcomes in Australian and New Zealand ICUs is uncertain.

**Objectives:** To measure the association of these processes in ICU with in-hospital mortality.

**Methods:** The Australian and New Zealand Intensive Care Society (ANZICS) Adult Patient Database and Critical Care Resources registry were used to extract patient-level factors, ICU-level factors and the year in which each process took place. Descriptive statistics and hierarchical logistic regression were used to determine the relationship between each process and in-hospital mortality.

**Results:** The study included 799 901 adults admitted to 173 ICUs from July 2009 to June 2016. The proportion of patients exposed to each process of care was 38.7% (antibiograms), 77.5% (AMS programmes) and 74.0% (ID rounds). After adjusting for confounders, patients admitted to ICUs that used ICU-specific antibiograms had a lower risk of in-hospital mortality [OR 0.95 (99% CI 0.92–0.99), P=0.001]. There was no association between the use of AMS programmes [OR 0.98 (99% CI 0.94–1.02), P=0.16] or routine rounds with ID physicians [OR 0.96 (99% CI 0.09–1.02), P=0.09] and in-hospital mortality.

**Conclusions:** Use of ICU-specific antibiograms was associated with lower in-hospital mortality for patients admitted to ICU. For hospitals that do not perform ICU-specific antibiograms, their implementation presents a low-risk infection management process that might improve patient outcomes.

# Introduction

Processes of care describe evidence-based systems, strategies and interventions that institutions employ to standardize and optimize best clinical practice. After implementation, these processes need to be evaluated to ensure they improve desired patient-centred outcomes.

Several infection management processes have been developed in response to climbing rates of MDR organisms associated with increased antibiotic prescribing.<sup>1,2</sup> The complex pathways that allow microbial resistance to develop require multidisciplinary input from a wide range of specialists including infectious diseases (ID) physicians, clinical microbiologists, pharmacists, infection control and relevant admitting specialty services.<sup>3,4</sup> The Australian Commission on Safety and Quality in Health Care 2018 recommended the implementation of antimicrobial stewardship (AMS) programmes for patient care. As a component of an AMS programme it advises the development of regional antibiograms.<sup>5</sup> Antibiograms describe tables of data that show the relative prevalence of key microbial species and corresponding rates of antimicrobial susceptibility of all isolates collected from a defined

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source. Within the ICU, additional interventions targeting the management of infections have been designed.

These include the routine involvement of ID physicians in the evaluation of culture results on clinical decision-making and the formulation of targeted ICU-specific, in addition to regional/hospital-wide, antibiograms. The impact of ICU-specific antibiograms, AMS programmes and routine input from ID physicians on patient-centred outcomes has not been extensively examined in Australia and New Zealand.<sup>6,7</sup> We hypothesized that patients admitted to ICUs in Australia and New Zealand that use these processes of infection management would have lower adjusted in-hospital mortality than patients admitted to ICUs that did not.

# Materials and methods

### Ethics

Access to data was granted by the Australian and New Zealand Intensive Care Society (ANZICS) Centre for Outcome and Resource Evaluation (CORE) Management Committee in accordance with standing protocols. The project was approved by The Alfred Human Research and Ethics Committee and due to the retrospective de-identified nature of the data used, patient consent was not required (reference number 566/19).

### Study design and oversight

We conducted a retrospective cohort study using data from the ANZICS Adult Patient Database and the Critical Care Resources Registry.<sup>8</sup> The ANZICS Adult Patient Database collects de-identified data submitted on a quarterly basis for benchmarking purposes from approximately 90% of the ICUs in Australia and New Zealand and presently contains more than 2.5 million individual ICU admission episodes. Australian and New Zealand ICUs are also surveyed each year for the Critical Care Resources Registry about the provision and utilization of critical care resources. Between 2009 and 2016, the following three questions were asked about each ICU for each financial year (July to June):

- 1. Does the unit regularly obtain antibiograms specific to ICU (rather than hospital-wide antibiograms)?
- 2. Does the unit have an ongoing AMS programme?
- 3. Does the unit have routine rounds with an ID physician and/or microbiologist?

### Study population

All patients admitted to an ICU that reported to both the Adult Patient Database and the Critical Care Resources Registry between July 2009 and June 2016 were included. Patients were excluded if their survival outcome was missing or they were admitted for palliative care/potential organ donation. To avoid double counting of the primary outcome, patients transferred to another ICU (i.e. an unknown survival outcome) and readmission episodes to ICU within the same hospital stay were excluded.

### Exposures and outcomes

The characteristics and outcomes of patients within ICUs each year undertaking each of the three processes above were compared with patients in ICUs that did not. We examined the number of ICUs reporting each process and changes in proportionate patient numbers within these ICUs over time. Patient demographics recorded included age, ICU admission diagnosis, invasive mechanical ventilation, elective surgical status, severity of illness assessed by APACHE II and III scores and the Australian and New Zealand risk of death (ANZROD). ANZROD is a bi-nationally derived mortality prediction model, which includes age, acute physiological disturbance, elective surgical status, chronic comorbidities and the presence of treatment limitations. It employs separate regression equations for each major diagnostic group and adjustments for each specific admission diagnosis within each group. It provides accurate mortality prediction for Australian and New Zealand ICU patients, is well calibrated and highly discriminatory, with an area under the receiver operating characteristic curve (AUROC) of >0.9 when applied to the overall ICU population.<sup>9,10</sup> ICU-level factors included type of hospital (rural/regional, metropolitan, tertiary and private). The primary outcome examined was in-hospital mortality. Other outcomes included mortality in ICU, readmission to ICU, length of stay in ICU and hospital.

### Statistical analysis

Univariable comparisons were performed using chi-squared tests for categorical data, *t*-tests for normally distributed data and Wilcoxon rank-sum and Kruskal–Wallis tests for non-parametric data, with results reported as percentages and counts, mean/SD or median/IQR, respectively.

Hierarchical logistic regression was used to determine associations with the primary outcome (in-hospital mortality) with patients nested within sites and sites treated as a random effect. Other independent variables were entered as fixed effects. Individual patient factors adjusted for included severity of illness (estimated using ANZROD) and year of admission to ICU. Hospital-level factors included region/hospital type as well as the three processes as exposures of interest in the same regression model. Model discrimination was assessed using the AUROC. Brier scores were reported to describe overall model performance including calibration.

Sensitivity analyses were undertaken examining only ICUs that consistently reported to both the Adult Patient Database and the Critical Care Resources Registry every year throughout the study period, by examining ICUs that did not report to the databases consistently throughout the study period, by adding time spent in ICU as an independent variable to the regression models to control for potential duration of exposure, by repeating regression models for each individual process of care and by examining pre-specified subgroup pairs, which included ventilated versus non-ventilated patients and patients admitted to ICU with a primary diagnosis related to infection (Table S1, available as Supplementary data at JAC Online) versus those admitted with non-infective diagnoses.

Given the large sample size and multiple comparisons undertaken, a two-sided *P* value of <0.01 was considered significant to increase the robustness of the study. Results were reported as OR with 99% CI. Statistical analyses were performed using Stata 16.1 (College Station, TX, USA) and SAS software version 9.4 (SAS Institute, Cary, NC, USA), with multivariable logistic regression models constructed using the melogit command in Stata.

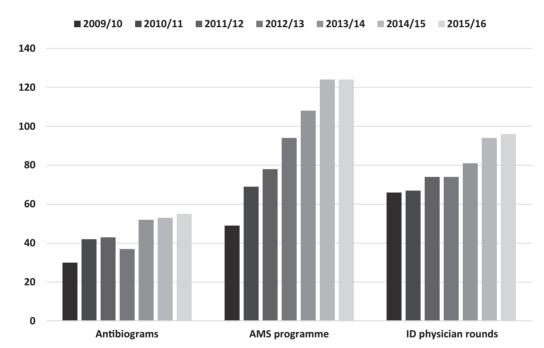
# Results

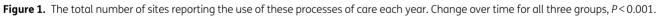
The study cohort consisted of 799 901 (85% of all admissions reported to the Adult Patient Database) patients admitted between July 2009 and June 2016 to 173 ICUs in Australia and New Zealand (Figure S1). The least frequently reported process was the use of ICU-specific antibiograms, with 96 (55.5%) ICUs reporting their use in at least 1 year and 17 (9.8%) ICUs reporting their use every year. This was followed by routine rounds with ID physicians, with 68 (39.3%) ICUs reporting their use in at least 1 year and 46 (26.6%) ICUs reporting their use every year. The most common process measure reported was an AMS programme, with 99 (57.2%) ICUs reporting their use in at least 1 year and 58 (33.5%) ICUs reporting their use in at least 1 year and 58 (33.5%) ICUs reporting their use in at least 1 year and 58 (33.5%) ICUs reporting their use in at least 1 year and 58 (33.5%) ICUs reporting their use in at least 1 year and 58 (33.5%) ICUs reporting their use hospital ICUs (Table 1). Over the study period, there was a progressive increase in the number of

Hospital classifications	Total	Regional	Metropolitan	Tertiary	Private
Number of sites	173	41	36	40	56
Antibiograms, <i>n</i> (%)					
Never	58 (33.5)	14 (34.1)	16 (44.4)	8 (20.5)	20 (36.4)
Every year	17 (9.8)	1 (2.4)	4 (11.1)	6 (15.4)	6 (10.9)
≥1 year <sup>a</sup>	96 (55.5)	26 (64.4)	16 (44.4)	25 (64.1)	29 (52.7)
AMS programme, <i>n</i> (%)					
Never	14 (8.1)	1 (2.4)	3 (8.1)	0	10 (18.2)
Every year	58 (33.5)	11 (26.8)	11 (30.6)	25 (64.1)	11 (20)
≥1 year <sup>a</sup>	99 (57.2)	29 (70.7)	22 (61.1)	14 (35.9)	34 (61.8)
Rounds with ID physician, n (%)					
Never	46 (26.6)	18 (43.9)	2 (5.6)	0	26 (47.3)
Every year	67 (38.7)	8 (19.5)	18 (50)	35 (89.7)	6 (10.9)
≥1 year <sup>a</sup>	68 (39.3)	15 (36.6)	16 (44.4)	14 (35.9)	23 (41.8)

Table 1. Proportion of sites reporting each process of care over the course of the study

<sup>a</sup>Excluding sites reporting the use of these processes every year.





sites (Figure 1) and an increase in the proportion of overall patient admissions to sites reporting each process (Figure 2).

The demographics of patients admitted to all ICUs overall and for each site designation have been included in Table S2.

### ICU-specific antibiograms

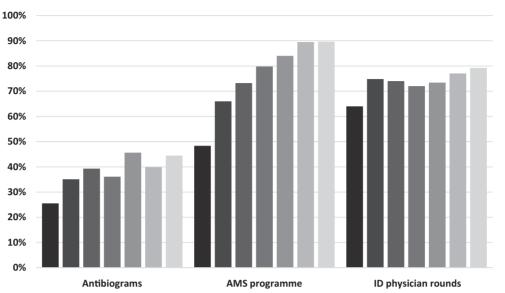
In-hospital mortality was lower in the ICU-specific antibiogram group (8.7% versus 8.9%, P < 0.001) despite having a greater level of acute physiological disturbance (as evidenced by higher acute physiology subscores) (Table 2). After adjusting for confounders, admission to ICUs reporting the use of ICU-specific antibiograms

### AMS programmes

Observed in-hospital mortality was higher in the AMS group (9.2% versus 7.5%, P < 0.001), which corresponds to the greater level of acute physiological disturbance seen in this group (Table 2). After adjusting for confounders, there was no significant association with the use of AMS programmes in ICU and in-hospital mortality [OR 0.98 (99% CI 0.94–1.02), P=0.16] (Table 3).

was independently associated with a reduced in-hospital mortality

[OR 0.95 (99% CI 0.92-0.99) P = 0.001] (Table 3).



■ 2009/10 ■ 2010/11 ■ 2011/12 ■ 2012/13 ■ 2013/14 ■ 2014/15 ■ 2015/16

**Figure 2.** The annual proportion of total ICU admissions to units that reported the use of each process of care. Change over time for all three groups, *P*<0.001.

Table 2. The reported use of processes of care in ICU and thei	r corresponding patient demographics
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Interventions	Antibiograms		AMS programme		Rounds with ID physician	
	Yes	No	Yes	No	Yes	No
Demographics						
Patient admissions, n	301 346	477 744	606 695	176157	584212	205 464
Age, years, median (IQR)	63.3 (47.7-74.0)	) 64.7 (49.7–75.5)	63.5 (48.0-74.4)	66.1 (52.2-76.5	) 63 (47.5–74)	67 (53.3–77.2)
$\geq 2$ chronic comorbidities, % ( <i>n</i> )	6.6 (19917)	7.1 (33 755)	6.7 (40 751)	7.4 (13 113)	7.2 (42 146)	6.0 (12 261)
Elective surgical admissions, % (n)	44.5 (134 110)	42.5 (202 430)	41.1 (248 743)	51.1 (89 953)	39.2 (228 273)	55 (112 977)
Admission diagnosis related to infection, % (n)	11.5 (34 992)	12.7 (60 666)	12.8 (77 490)	10.5 (18 556)	13.0 (75 749)	10.4 (21 423)
Patients ventilated on Day 1 of ICU admission, % (n)	43.1 (129 273)	35.7 (170 569)	40.7 (247 075)	30.6 (53 519)	43.1 (251 457)	24.6 (50 494)
Illness severity scores						
APACHE II score, mean (±SD)	15.6 (±8.0)	15.5 (±7.7)	15.8 (±7.9)	14.8 (±7.4)	16.0 (±8.0)	14.2 (±7.2)
APACHE III overall score, mean (±SD)	54.1 (±26.4)	53.2 (±25.9)	54.3 (±26.4)	50.6 (±24.7)	55.0 (±26.7)	48.9 (±23.7)
APACHE III acute physiology subscore, mean (±SD)	42.3 (±25.1)	41.4 (±24.1)	42.7 (±25.0)	38.4 (±22.6)	43.5 (±25.2)	36.6 (±21.4)
Predicted risk of death,	8.6, 1.7	8.4, 1.8	8.9, 1.9	7.0, 1.4	9.3, 2.0	6.1, 1.3
ANZROD (%), mean, median (IQR)	(0.5-7.1)	(0.6–7.3)	(0.6–7.8)	(0.5–5.4)	(0.6-8.3)	(0.4-4.5)
Outcomes						
Died in hospital, % (n)	8.7 (26 215)	8.9 (42 662)	9.2 (55 868)	7.5 (13 299)	9.7 (56 628)	6.4 (13 097)
Died in ICU, % (n)	5.7 (17 143)	5.7 (27 089)*	6.0 (36 294)	4.6 (8124)	6.3 (36 968)	3.8 (7785)
ICU length of stay, days, median (IQR)	1.7 (0.9–3.1)	1.8 (0.9–3.5)	1.8 (0.9–3.5)	1.7 (0.9–3.0)	1.8 (0.9–3.6)	1.7 (0.9–2.9)
Hospital length of stay, days, median (IQR)	8.3 (4.7–15.2)	8.4 (4.6–15.5)	8.5 (4.7–15.8)	8.1 (4.5–14.3)	8.7 (5.0–16.4)	7.5 (4.1–13.0)
Readmission to ICU, % (n)	4.5 (13 567)	4.5 (21 593)**	4.6 (27 909)	4.2 (7349)	4.8 (27 789)	3.7 (7667)

\*P=0.52; \*\*P=0.72. P<0.001 for all other differences between patients exposed to antibiograms, an AMS programme or ID physician rounds.

	OR (99% CI)	P value
Exposure		
Antibiograms	0.95 (0.92–0.99)	0.001
AMS programme	0.98 (0.94-1.02)	0.16
Rounds with ID physician	0.96 (0.90-1.02)	0.09
Severity		
Predicted risk of death (ANZROD)	1.07 (1.07-1.08)	< 0.001
Site		
Rural/regional	1.0 (reference value)	
Metropolitan	1.08 (0.89-1.32)	0.30
Tertiary	1.11 (0.91–1.34)	0.18
Private	0.58 (0.48-0.70)	< 0.001
Year		
2009/2010	1.0 (reference value)	
2010/2011	0.96 (0.91-1.01)	0.03
2011/2012	0.91 (0.86–0.96)	< 0.001
2012/2013	0.87 (0.83-0.92)	< 0.001
2013/2014	0.83 (0.79–0.88)	< 0.001
2014/2015	0.85 (0.81–0.89)	< 0.001
2015/2016	0.81 (0.78-0.86)	< 0.001

**Table 3.** Hierarchical logistic regression model for factors associated with in-hospital mortality

Number of observations = 762 356; AUROC = 0.90; Brier score = 0.055; variance (site) = 0.072 (99% CI 0.052–0.1).

### Routine rounds with ID physicians

Observed in-hospital mortality in the group reporting routine rounds with ID physicians was higher (9.7% versus 6.4%, P<0.001), consistent with the greater level of acute physiological disturbance seen in this group (Table 2). After adjusting for confounders, there was no significant association between the reported use of routine rounds with ID physicians and in-hospital mortality [OR 0.96 (99% CI 0.90–1.02), P=0.09] (Table 3).

# Sensitivity analyses

Similar findings were obtained when length of stay in ICU was included in the regression model to adjust for time exposed to each specific process; antibiograms were still associated with improved in-hospital mortality [OR 0.96 (99% CI 0.92–0.99), P=0.002] whereas AMS programmes and routine rounds with ID physicians were not [OR 0.98 (99% CI 0.94–1.02), P=0.16 and 0.96 (0.90–1.02), P=0.1, respectively] (Table S3).

When analyses were restricted to only those hospitals that reported consistently to both databases every year, similar trends were observed but mortality benefit associated with antibiograms [OR 0.97 (99% CI 0.93–1.01), P=0.028] and AMS programmes [OR 0.94 (99% CI 0.87–1.02), P=0.045] did not reach the significance level set for this study (Table S4).

When analyses were restricted to hospitals that did not consistently contribute data for the whole study period, the findings were consistent with the overall findings, showing an in-hospital mortality benefit associated with antibiograms [OR 0.91 (99% CI 0.83– 0.998), P=0.009] (Table S5). When each process of care was modelled individually the results remained consistent with the overall

findings. The use of antibiograms was associated with improved in-hospital mortality [OR 0.96 (99% CI 0.92–0.99), P=0.002] and there was no difference in outcomes with the use of AMS programmes [OR 0.97 (99% CI 0.93–1.01), P=0.06] or rounds with ID physicians [OR 0.96 (99% CI 0.90–1.02), P=0.05] (Tables S6–S8).

# Subgroup analyses (ventilated and non-ventilated, infective and non-infective admission diagnoses)

Patients who were ventilated on Day 1 of admission had lower adjusted in-hospital mortality if they were admitted to ICUs that used ICU-specific antibiograms. There was no association between mortality and the use of AMS programmes or rounds with ID physicians (Table 4 and Table S9). For inpatients who were not ventilated on Day 1 of admission, there was no association between adjusted in-hospital mortality and the use of any of these processes (Table 4 and Table S10). For inpatients admitted with diagnoses related to infection, there was no association between adjusted in-hospital mortality and the use of any of these processes (Table 4 and Table S11). Patients admitted with diagnoses unrelated to infection had a lower adjusted in-hospital mortality if they were admitted to ICUs that used ICU-specific antibiograms or AMS programmes. There was no association identified in this group with routine rounds by ID physicians (Table 4 and Table S12).

# Discussion

# Summary of findings

In this retrospective cohort study of almost 800000 patients admitted to 173 ICUs in Australia and New Zealand we observed a consistent increase in the number of sites reporting the use of all three infection management processes over the study period. The implementation of ICU-specific antibiograms was the least commonly reported intervention. AMS programmes and routine rounds with ID physicians were reported by the majority of sites. We observed lower adjusted in-hospital mortality for patients admitted to ICUs who reported the use of ICU-specific antibiograms. There was no significant association found between the use of either AMS programmes or routine rounds with ID physicians and adjusted in-hospital mortality.

# Relation to published literature

Geographically distinct ICUs within a single hospital have been reported to yield unique microbial flora and resistance patterns when antibiogram data are collected and evaluated separately by source of origin. Similar findings have been observed between ICU-specific and hospital-wide antibiograms.<sup>11,12</sup> Formulating empirical antimicrobial strategies on location-specific antibiograms has been shown to improve times between clinical diagnosis and the surrogate marker 'adequate antibiotic coverage' in the therapy of ICU patients.<sup>13</sup> Delay in correct antimicrobial coverage of patients with sepsis has been associated with increased mortality.<sup>14</sup> We examined whether the performance of ICU-specific antibiograms would translate into overall improvements in patient-centred outcomes such as in-hospital mortality.

AMS programmes have been shown to improve guideline adherence and reduce antibiotic prescribing, course duration, antimicrobial drug resistance rates, costs and length of stay but

Table 4. Hierarchical loa	istic regression model for factors as	ssociated with in-hospital mortalit	v subaroup analysis summary <sup>a</sup>
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Subgroup and process	Observed mortality (process present)	Observed mortality (process absent)	Adjusted OR (99% CI)	P value
Ventilated (total = 304 725), % (n/	/N)			
Antibiograms	13.2 (17 128/129 273)	14.3 (24 428/170 569)	0.949 (0.904–0.997) <sup>b</sup>	0.007
AMS programme	14.2 (35 083/247 075)	12.3 (6628/53 519)	0.96 (0.88-1.05)	0.29
Rounds with ID physician	14.3 (36 203/251 457)	11.4 (5745/50 494)	0.99 (0.93-1.05)	0.55
Not ventilated (total = 494 028), %	6 (n/N)			
Antibiograms	5.3 (9035/170947)	5.9 (18 233/307 153)	0.96 (0.90-1.01)	0.047
AMS programme	5.8 (20 783/359 851)	5.4 (6620/121 529)	0.97 (0.90-1.06)	0.38
Rounds with ID physician	6.1 (20 372/331 620)	4.7 (7352/154 957)	0.98 (0.92-1.04)	0.44
ICU admission diagnosis related t	o infection (total = 98 542), % ( <i>n/N</i>	)		
Antibiograms	16.3 (5692/34 992)	15.6 (9494/60 666)	1.00 (0.93-1.08)	0.97
AMS programme	15.9 (12 323/77 490)	15.7 (2907/18 556)	1.08 (0.96-1.21)	0.1
Rounds with ID physician	16.5 (12 482/75 749)	13.6 (2918/21 423)	0.99 (0.91-1.08)	0.77
ICU admission diagnosis not relat	ed to infection (total = 701 359), %	5 (n/N)		
Antibiograms	7.7 (2918/21 423)	7.9 (33 168/417 078)	0.94 (0.90-0.99)	0.001
AMS programme	8.2 (43 545/529 475)	6.6 (10 392/157 601)	0.930 (0.868–0.997) <sup>b</sup>	0.007
Rounds with ID physician	8.6 (44 146/508 463)	5.5 (10179/184041)	0.97 (0.92–1.02)	0.08

<sup>a</sup>The full multivariable analyses tables for the four cohorts summarized, including corrections for predicted risk of death (ANZROD), site and year of admission, can be found in Tables S4–S7.

<sup>b</sup>Reported to three decimal places for clarity.

without a clear impact on mortality in the general hospital population.<sup>6,15-17</sup> Several studies show that consultation of ID physicians for highly specific patient subpopulations in hospital, such as those with blood culture-proven candidaemia and *Staphylococcus* aureus bacteraemia, improves compliance with evidence-based treatment and investigations, with an associated improvement in hospital length of stay and patient mortality.<sup>18-20</sup> Routine collaboration with ID physicians in critical care settings in small singlecentre studies has been shown to improve guideline adherence, optimize antimicrobial use and reduce costs, while patients benefit from a lower number of days ventilated, shorter hospital length of stay and improved in-hospital mortality.<sup>21,22</sup> Our study evaluated the impact associated with these processes on in-hospital mortality of a large population of ICU patients, encompassing all ICU admission diagnoses at 173 sites and adjusted for relevant confounders.

### Interpretation

Our findings suggest that improved outcomes for ICU patients may be achieved with formulation of ICU-specific antibiograms that represent the unique patterns of flora and resistance from each ICU. Having access to this information may aid decision-making for antimicrobial prescribing and the formulation of empirical regimens to optimally manage infections in the ICU. Since ICUspecific antibiograms were the least commonly reported process in our study, this represents an opportunity for improvement that is not available with other more ubiquitous strategies such as AMS programmes. While our study suggests findings are applicable to all ICUs we recognize that ICU-specific antibiograms may be difficult to implement and less reliable in smaller ICUs with lower numbers of infections.<sup>23</sup> The lack of a difference in mortality with the use of AMS programmes and routine rounds with ID physicians is still an important finding. It shows that previously proven benefits of these processes such as reduced costs and microbial resistance rates do not come at any increased risk to the overall ICU patient population.

The subgroup that appeared to benefit most from being in an ICU that performed ICU-specific antibiograms or had an AMS programme was those admitted with a diagnosis unrelated to infection. Although this may initially seem counterintuitive, patients with causes of admission related to infection, such as pneumonia, would have developed these infections in the community and should have received diagnosis-specific guideline-based treatments built on community antibiograms, which could explain the lack of benefit observed with ICU-specific antibiograms in this group. ICU-specific antibiograms and AMS programmes may have led to shorter times before adequate antimicrobial coverage and quicker response to therapy for infections developed after admission to ICU thereby contributing to better outcomes. There is also potentially an increased incidence of referrals to ID physicians and their involvement in ongoing patient care under these circumstances, which cannot be accounted for in this study.

#### Strengths and weaknesses

The large sample size, representing the majority (85%) of total admissions reported to the Adult Patient Database, is likely representative of the true ICU patient population and the findings widely applicable in ICUs in Australia and New Zealand. Accurate clinical data allowed robust risk adjustment for available confounders that might have influenced the association between each process and in-hospital mortality. The findings were similar across all sensitivity analysis.

This is a retrospective cohort study, which can only demonstrate association not causation. There is wide variation in clinical practice associated with the use of each of these processes across different sites. We cannot ascertain which specific processes individual patients received. Nor can we determine what other treatments patients received, only that they were in an ICU that reported the use of these processes during that time period. While the performance of ICU-specific antibiograms could theoretically allow the generation of more targeted empirical regimens, minimizing time until appropriate antibiotic coverage and minimizing unnecessary broad-spectrum therapy, management of individual patients was not reported and cannot be assumed.

In addition, ICUs that implement ICU-specific antibiograms may also have other unrelated factors that impact on patient outcomes that were not assessed in this study. By examining all ICU admissions, it is possible that the inclusion of patients who were unlikely to either benefit from or who were unlikely to be significantly exposed to these processes (e.g. overnight admissions for elective surgery) may have 'dampened' the treatment effect. The lack of a detectable overall association between mortality and AMS programmes or routine rounds with ID physicians may have been influenced by the fact that almost all sites were already performing them.

### Implications for future research

More in-depth research is required to determine how antibiograms, AMS programmes and routine ID physician rounds (independently or in combination) influence treatment delivered to individual patients. Prospective analysis to measure improvements before and after the introduction of these process measures should be performed, including cost-benefit analysis.

### Conclusions

Use of ICU-specific antibiograms was associated with lower inhospital mortality for patients admitted to ICU. For hospitals that do not perform ICU-specific antibiograms, their implementation presents a low-risk infection management process that might improve patient outcomes.

# Acknowledgements

We acknowledge the ANZICS CORE for providing the data used in the current study. We and the ANZICS CORE management committee would like to thank clinicians, data collectors and researchers from all the contributing sites listed in Table S13.

# Funding

This research was carried out as part of our routine work.

# Transparency declarations

None to declare.

# Supplementary data

Tables S1 to S13 and Figure S1 are available as Supplementary data at JAC Online.

# References

**1** Costelloe C, Metcalfe C, Lovering A *et al*. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *BMJ* 2010; **340**: c2096.

**2** Turnidge J. Antimicrobial use and resistance in Australia. *Aust Prescr* 2017; **40**: 2–3.

**3** Struelens MJ. The epidemiology of antimicrobial resistance in hospital acquired infections: problems and possible solutions. *BMJ* 1998; **317**: 652–4.

**4** Struelens MJ. Multidisciplinary antimicrobial management teams: the way forward to control antimicrobial resistance in hospitals. *Curr Opin Infect Dis* 2003; **16**: 305–7.

**5** Australian Commission on Safety and Quality in Health Care. Antimicrobial Stewardship in Australian Health Care 2018. 2018. https://www.safetyand quality.gov.au/sites/default/files/migrated/AMSAH-Book-WEB-COMPLETE.pdf.

**6** Davey P, Marwick CA, Scott CL *et al*. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev* 2017; issue **2**: CD003543.

**7** Schuts EC, Hulscher M, Mouton JW *et al.* Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis. *Lancet Infect Dis* 2016; **16**: 847–56.

**8** Stow PJ, Hart GK, Higlett T *et al.* Development and implementation of a high-quality clinical database: the Australian and New Zealand Intensive Care Society Adult Patient Database. *J Crit Care* 2006; **21**: 133–41.

**9** Paul E, Bailey M, Pilcher D. Risk prediction of hospital mortality for adult patients admitted to Australian and New Zealand intensive care units: development and validation of the Australian and New Zealand Risk of Death model. *J Crit Care* 2013; **28**: 935–41.

**10** Pilcher D, Paul E, Bailey M *et al.* The Australian and New Zealand Risk of Death (ANZROD) model: getting mortality prediction right for intensive care units. *Crit Care Resusc* 2014; **16**: 3–4.

**11** Kaufman D, Haas CE, Edinger R *et al*. Antibiotic susceptibility in the surgical intensive care unit compared with the hospital-wide antibiogram. *Arch Surg* 1998; **133**: 1041–5.

**12** Namias N, Samiian L, Nino D *et al.* Incidence and susceptibility of pathogenic bacteria vary between intensive care units within a single hospital: implications for empiric antibiotic strategies. *J Trauma* 2000; **49**: 638–45; discussion 645–6.

**13** Randhawa V, Sarwar S, Walker S *et al*. Weighted-incidence syndromic combination antibiograms to guide empiric treatment of critical care infections: a retrospective cohort study. *Crit Care* 2014; **18**: R112.

**14** Kumar A, Roberts D, Wood KE *et al.* Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med* 2006; **34**: 1589–96.

**15** Karanika S, Paudel S, Grigoras C *et al.* Systematic review and meta-analysis of clinical and economic outcomes from the implementation of hospital-based antimicrobial stewardship programs. *Antimicrob Agents Chemother* 2016; **60**: 4840–52.

**16** Malani AN, Richards PG, Kapila S *et al.* Clinical and economic outcomes from a community hospital's antimicrobial stewardship program. *Am J Infect Control* 2013; **41**: 145–8.

**17** Standiford HC, Chan S, Tripoli M *et al.* Antimicrobial stewardship at a large tertiary care academic medical center: cost analysis before, during, and after a 7-year program. *Infect Control Hosp Epidemiol* 2012; **33**: 338–45.

**18** Bai AD, Showler A, Burry L *et al.* Impact of infectious disease consultation on quality of care, mortality, and length of stay in *Staphylococcus aureus* bacteremia: results from a large multicenter cohort study. *Clin Infect Dis* 2015; **60**: 1451–61.

**19** Ishikane M, Hayakawa K, Kutsuna S *et al.* The impact of infectious disease consultation in candidemia in a tertiary care hospital in Japan over 12 years. *PLoS One* 2019; **14**: e0215996.

**20** Nagao M, Iinuma Y, Saito T *et al.* Close cooperation between infectious disease physicians and attending physicians can result in better management and outcome for patients with *Staphylococcus aureus* bacteraemia. *Clin Microbiol Infect* 2010; **16**: 1783–8.

**21** Raineri E, Pan A, Mondello P *et al.* Role of the infectious diseases specialist consultant on the appropriateness of antimicrobial therapy prescription in an intensive care unit. *Am J Infect Control* 2008; **36**: 283–90.

**22** Rimawi RH, Mazer MA, Siraj DS *et al*. Impact of regular collaboration between infectious diseases and critical care practitioners on antimicrobial utilization and patient outcome. *Crit Care Med* 2013; **41**: 2099–107.

**23** CLSI. Performance Standards for Antimicrobial Susceptibility Testing— Twenty-Third Edition: M100. 2013.