

Reduction of broad spectrum antibiotic use with computerised decision support in an intensive care unit

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Abstract

Objective To implement and evaluate the effect of a computerised decision support tool on antibiotic use in an intensive care unit (ICU).

Design Prospective before-and-after cohort study

Setting 24-bed tertiary hospital adult medical/surgical ICU

Participants All consecutive patients from May 2001-November 2001 (N=524) and March 2002 to September 2002 (N=536)

Intervention A real-time microbiology browser and computerised decision-support system for isolate directed antibiotic prescription

Main Outcome Measures Number of courses of antibiotic prescribed, antibiotic utilization (defined daily doses (DDDs)/100 ICU bed-days), antibiotic susceptibility mismatches, and system uptake.

Results There was a significant reduction in the proportion of patients prescribed carbapenems (Odds ratio= 0.61, 95% CI [0.39, 0.97], p=0.04), third generation cephalosporins (OR=0.58, 95% CI [0.42, 0.79], p=0.001) and vancomycin (OR=0.67, 95% CI [0.45, 1.00], p=0.05) after adjustment for risk factors including Apache II score, suspected infection, positive microbiology, intubation, and length of stay. The decision support tool was associated with a 10.5% reduction in both total antibiotic utilisation (166 to 149 DDDs/100 ICU bed-days) and the highest volume broad-spectrum antibiotics. There were fewer susceptibility mismatches for initial antibiotic therapy (OR=0.63, 95% CI [0.39,0.98], p=0.02) and increased de-escalation to narrower spectrum antibiotics. Uptake of the program was high with 6028 access episodes during the 6-month evaluation period.

Conclusions This tool streamlined collation and clinical use of microbiology results, and integrated into the daily ICU workflow. Its introduction was accompanied by a reduction in

both total and broad-spectrum antibiotic use and an increase in the number of switches to narrower spectrum antibiotics.

Introduction

Over half of intensive care unit (ICU) patients receive antibiotics during their admission [1] [2]. Inadequate antibiotic coverage has been shown to be associated with increased morbidity and mortality [3-5]. Diagnosis of infection on the basis of clinical suspicion may result in the prolonged administration of empiric broad-spectrum, expensive antibiotics, which impacts upon the rate of acquired antibiotic resistance [6]. Knowledge of an intensive care unit's most common bacterial isolates and their antibiotic susceptibility patterns facilitates effective empirical antibiotic therapy, and supports decisions to restrict or reduce the clinical availability of certain antibiotics [7]. Antibiotic interventions should aim to limit the emergence of antibiotic resistance whilst simultaneously improving patient outcomes and decreasing pharmaceutical costs [8].

Computerised decision support systems are promoted as an effective way to improve hospital antibiotic prescribing [9], as they have been shown to improve antibiotic selection (level 1/2 evidence)[10, 11], potentially reduce the emergence of antibiotic resistance (level 2 evidence)[12], and minimise antibiotic costs and length of hospitalisation. However, applicability of these findings to other institutions is limited due to the lack of transferability of these CDSS, the heterogeneity of study designs, and the potential publication bias from "home-grown" [13, 14] systems. There are a few reports of stand-alone pharmacy based programs that monitored microbiology results and antibiotic use[15-17], but antibiotic decision support systems are rarely utilised in hospitals without computerised physician order entry [18]. Even with the most advanced decision support systems, prescribers may not follow more than one-third of offered antibiotic recommendations [10, 11].

We describe the evaluation of an ICU-based decision support system that provides real-time microbiology results and patient specific antibiotic recommendations for clinical isolates. We hypothesized that the ADVISE (Antibiotic Decision support for the Victorian Infectious Diseases Service) would significantly influence the pattern of ICU antibiotic use.

Materials and Methods

Setting

The Royal Melbourne Hospital is an adult tertiary hospital with a 24-bed combined medical, surgical and trauma ICU. The senior ICU medical staff regarded the overall pattern of antibiotic use and expenditure as an important gauge of clinical quality within the unit.

Intervention

The ADVISE program is a computerised decision support system for antibiotic prescription in the ICU that was developed by a group comprising infectious diseases physicians, intensive care physicians, and pharmacists. User-centred design methodology [19] identified the key functional requirements of improved searching and collation of microbiology results, education about the clinical epidemiology of isolates and optimal antibiotic prescription for potential pathogens. The ADVISE program was linked to the hospital pathology system and provided a real-time browser that allowed sorting and printing of microbiology reports for ward-rounds. For example, all microbiology results for a particular patient could be viewed on a single screen and sorted by date, site or culture result. Rule-based algorithms for treatment were written for each isolate and used the clinical site of the specimen (e.g blood, sputum), susceptibility profile, and patient allergies. Antibiotic recommendations were based on widely used infectious diseases resources [20, 21]. When laboratory susceptibilities were

not available, the program was able to suggest antibiotics on the basis of local antibiotic susceptibility data. Each isolate algorithm provided information about the characteristic clinical features and antibiotic susceptibility profile of the organism, as well as advisory comments recommending infection control notification or recommendation for infectious diseases service review. Clicking on an isolate/pathogen in the browser window generated the treatment recommendations. A comprehensive antibiotic database provided appropriate dose and dosing intervals for selected antibiotics, as well as dose modifications according to renal and hepatic dysfunction. Where antibiotic dosage depended on renal function, calculation of creatinine clearance automatically extracted the plasma creatinine level from the pathology clinical information system. On-screen in ADVISE the user could select actual or potential pathogens and compare these to one or many potential antibiotics, so that an overall antibacterial coverage pattern could be visualised.

Implementation of the system

Education about the program was provided by a written manual and through demonstrations to individuals and groups of medical staff during ICU teaching seminars. The ICU pharmacist also played an important role through frequent informal teaching and encouragement in the use of the system. Junior medical staff rotated through the unit every three months, advanced trainees every 6-12 months, while six permanent attending physicians conducted all ward rounds. No other antibiotic or infection control interventions were introduced during the period of the study. The ADVISE microbiology browser did not replace the existing pathology browser which was still available.

Outcome measures

The main outcome measures for this study were changes in the numbers of patients prescribed target antibiotics (broad-spectrum antibiotics carbapenems and ceftriaxone, and vancomycin)

and rates of overall antibiotic usage and broad-spectrum antibiotic usage, measured as the number of defined daily doses (DDDs) per 100 occupied ICU bed-days. Secondary outcomes included the number of antibiotic susceptibility mismatches during initial and directed therapy for both sterile and non-sterile isolates, the time to prescription of a microbiologically-appropriate antibiotic, and the proportion of cases where potential existed to use a narrower spectrum antibiotic. Access of ADVISE and its components was monitored electronically.

Study Design

A before-and-after study design was used to assess the impact of this program on antibiotic utilisation in the ICU. The 6-month pre-intervention study began in May 2001 whilst the 6-month post-implementation study was commenced in March 2002, 4 months after ADVISE was first deployed.

All patients admitted to the ICU (excluding routine cardiothoracic surgical patients) were followed from their date of admission to discharge from ICU (or death). Details of all positive bacterial cultures and antibiotic prescription during the ICU admission were recorded. The reason for commencement of antibiotic therapy was classified according to the clinical context as surgical prophylaxis, suspected infection or documented infection. Suspected infection required that the patient fulfilled the Systemic Inflammatory Response Syndrome (SIRS) Criteria [22] in the absence of a microbial isolate from a clinical sample. The use of antivirals and antifungals were not recorded, as these were not targets of the intervention.

Analysis was restricted to bacterial isolates for which results became available while the patient was in the ICU. Isolates from blood, sterile fluids, and tissue were referred to as “Sterile” and isolates from sputum, pus, urine, wound swabs and catheter tip cultures were classed as “Non-sterile”. Each isolate from a sterile site was included in the analysis, unless

the same organism with the same susceptibility pattern had been already isolated from the same site within 24 hours. Isolates from non-sterile sites were included only once if the same organism with the same susceptibility profile was isolated from the same site within a three-day period. In order to avoid the need to interview ICU clinical staff and therefore potentially influence their prescribing patterns, all bacteria reported by the laboratory were assumed to be clinically significant. Detailed clinical diagnostic information was not collected as this was beyond the scope of the present study.

Untreated isolates were defined as isolates not associated with any antibiotic therapy from their date of identification to 7 days following the release of antibiotic susceptibility results. Antibiotic susceptibility mismatches were evaluated twice; once for initial therapy (after organism identification but before susceptibility results) and once for directed therapy (after the release of laboratory susceptibility results). Delayed therapy was defined as adequate antibiotic therapy that was commenced greater than 24 hours after microbial identification or antibiotic susceptibilities were known. Rules were generated to standardise the interpretation of antibiotic therapy. If susceptibility results were not available, the antibiotic therapy (or coverage) was deemed to be adequate (no mismatch) if >75% of isolates would be expected to be susceptible to the antibiotic used, as determined from the local ICU antibiotic susceptibility profile over the preceding six-month period. This project was in accord with the hospital's ethics committee requirements for Quality Assurance projects at the time of this study.

Analysis

Overall antibiotic use was compared in terms of DDDs per 100 ICU bed-days, where DDDs = (total amount of antibiotic in grams)/(defined daily dose in grams [World Health Organisation #2554]). A multivariable binary logistic regression model was used to evaluate the change in

the proportion of patients commenced on a particular antibiotic (at any time during their stay) before and after the intervention. The model was performed for all the most commonly used antibiotics and included variables (selected a priori) that were believed to be prognostic or to influence antibiotic prescribing. Intervention group (pre- or post-) was included as an independent variable. Apache II score and age were treated as continuous variables, and length of stay was log-transformed. Suspected infection, gender, repeat admission to ICU, positive microbiology, intubation, admitting unit type (medical vs. surgical), and ICU mortality were included as categorical variables. Antibiotic susceptibility mismatches and de-escalation were compared in terms of risk ratios. Odds ratios (ORs) are given with 95% confidence intervals (CIs).

Results

The study sample consisted of 1060 ICU admissions (986 patients) between May 2001 and September 2002. Of these, 524 admissions (489 patients, 2209 patient-days) occurred before the intervention (pre-intervention) and 536 admissions (497 patients, 2285 patient days) after the intervention. Patient characteristics are shown in Table 1. Patients in the intervention cohort had higher APACHE scores (mean score 16.4 versus 13.8). The proportion of patients receiving antibiotics and proportion with suspected or documented infection were similar in both groups.

Impact on antibiotic use

Table 2 shows the proportions of patients treated with the most commonly used antibiotics. On univariable analysis, third generation cephalosporins use was significantly reduced and erythromycin use was significantly increased. The impact of risk factors for antibiotic use for the highest volume antibiotics prescribed is shown in Table 3. Patients from medical admitting units were more likely to receive ceftriaxone, whereas sicker patients or those requiring readmission were more likely to receive vancomycin and carbapenems.

After adjustment for potential confounders or risk factors for antibiotic use, there was a significant reduction in the number of prescribed courses of 3rd generation cephalosporins, carbapenems and vancomycin during the intervention (Table 4). We also tested the regression model for vancomycin with 'MRSA' as an alternative to 'positive microbiology' as a covariate to evaluate the impact of reduced MRSA isolates in the intervention cohort. The treatment effect was similar but did not reach significance (OR = 0.71, 95% CI [0.48, 1.05], p=0.09). Erythromycin use was most strongly associated with medical patients (OR= 7.99,

95% CI [4.95, 12.9], $p < 0.001$) as well as increased age, suspected infection, increased length of stay and being in the intervention group (OR=2.03, 95% CI [1.34-3.09], $p = 0.001$)

After ADVISE was deployed, total antibiotic usage decreased from 167 to 149 DDDs/100 ICU bed-days. There was reduction in the use of third generation cephalosporins (35.4 to 26.6 DDDs/100 bed-days), and carbapenems (21.4 to 16.9 DDDs/100 bed-days), which were the highest volume broad-spectrum agents and accounted for 25% of all antibiotics used in the unit. The change in antibiotic use conferred a potential annual cost savings of AU\$20,000.

Impact on antibiotic susceptibility mismatches

There were fewer isolates in the intervention cohort (303 vs. 237, RR=0.76, 95% [0.64, 0.91], $p = 0.002$). Nosocomial acquired isolates accounted for 90% of isolates in each group.

Respiratory isolates represented more than half of all isolates, and were more frequent in the intervention cohort (55% pre-intervention vs. 62% intervention, $p = 0.04$). There was no proportion of sterile site (blood, CSF, other sterile fluid) isolates were similar in both groups (20% pre-intervention vs. 19% intervention). The proportion of gram-positive bacteria was 50.5% and 48% in the pre-intervention and intervention cohorts respectively ($p = 0.54$).

Staphylococcus aureus was the most common isolate (38.3% pre-intervention vs. 34.6% intervention) however the proportion of *Staphylococcus aureus* that were methicillin resistant fell from 78% to 59% in the intervention cohort ($p < 0.001$). The most common isolates in both groups were coagulase negative Staphylococci, *Pseudomonas aeruginosa*, *Acinetobacter* spp., and *Escherichia coli*.

The baseline rate of adequate initial and directed antibiotic coverage for all isolates was 75.6% and 82.9% respectively. For sterile isolates, the baseline rate of adequate initial and directed antibiotic coverage was 88.6% and 96.7% respectively. Few isolates were untreated.

The program did not significantly change time to adequate therapy. Examining the impact of ADVISE on initial antibiotic choice after identification, there was a significant reduction in the number of susceptibility mismatches (OR=0.63, 95% CI [0.39, 0.98], p=0.02)(Table 3). There was no significant difference in mismatches for directed therapy (OR=1.12, 95%CI [0.73,1.68], p=0.02). More isolates were associated with a reduction in antibiotic spectrum during directed therapy in the intervention group (OR = 2.20, 95% CI [1.17, 4.11], p=0.01).

Uptake of ADVISE

During the 6-month intervention period, the microbiology browser was used 6028 times (median 3 episodes/patient/day). There were 290 microbiology algorithms viewed, and 250 episodes of antibiotic database use.

Discussion

Our study has demonstrated that the introduction of an antibiotic decision support tool into the ICU was associated with measurable improvements in antibiotic use and ready integration into the workflow with over 6000 episodes of use during the 6-month intervention period. We believe that the rapid physician acceptance and uptake was largely due to the additional feature of an effective browser and the substantial reduction in time usually taken to manage microbiology results for ward rounds. The decision support system was used on average three times a day for each patient, and became the preferred source of microbiology results despite the existing pathology interface remaining available.

ADVISE consists of several components including a browser, education resources, antibiotic recommendations, and dosing information. Each of these components may have influenced the clinical decision making, and it is difficult, using the simple evaluation results reported above, to know what combination of these was responsible for the changes observed [24]. Only a minority of patients had organisms isolated microbiologically, and yet over 60% received antibiotics, usually for clinically suspected infection, which is consistent with other studies of ICU antibiotic use [1] [2]. There was a significant reduction in the number of courses of carbapenems, ceftriaxone and vancomycin, the highest volume antibiotics, even after adjustment for the presence of positive microbiology, severity of illness and other factors influencing antibiotic prescribing. Although the difference in Apache scores was small, the higher scores in the intervention group would act in the direction (if any) of increase antibiotic use, as more seriously ill patients would be prescribed antibiotics.

Effective presentation of laboratory results can reduce unnecessary testing and reduce the costs of pathology [25]. The reduction in the number of microbiology isolates in the intervention group is likely to be due to decreased testing. The provision of real-time information about isolates, especially the more common ICU pathogens would have increased the collective knowledge and confidence of clinicians in the ICU regarding the choice of alternative antibiotic options (as well as discontinuing therapy). This benefit may explain the observed shift during the course of this study away from previously frequent choices, such as third generation cephalosporins and carbapenems, to quinolones and extended spectrum penicillins. The increased in the use of erythromycin in the intervention group was interesting and may be attributed to sicker patients with pneumonia. The intervention study period included the winter/influenza season when presentations with respiratory illnesses would be higher, reflected by the significantly increased number of respiratory isolates in this group.

The adequacy of prescribing for isolates during the pre-intervention period ranged from 88-97% for sterile isolates, and 80-85% for non-sterile isolates. This higher than expected coverage, in combination with the reduced number of isolates in the intervention period, led to a reduction in statistical power to find the differences between phases of this study in the adequacy of antibiotic choices as statistically significant. However, we were able to demonstrate two potential benefits of ADVISE, namely that there was no deterioration in the proportion of inadequately covered isolates despite the significantly reduced use of broad-spectrum antibiotics, and that there was increased de-escalation of initial therapy to narrower spectrum antibiotics.

There are a number of limitations to this study. The evaluation of computerised decision support systems in a real clinical setting is complex. Recommended methodology using a controlled trial where the randomisation occurs by physician [26] is not practical in the

critical care setting because there would be cross-contamination between clinicians. An alternative recommended method for evaluating the impact of hospital antibiotic interventions is the interrupted time series analysis using defined daily doses [27]. However, the presentation of defined daily doses of antibiotics over a short time (time-series) to measure change is potentially misleading, as it does not take into account adequacy of therapy, severity of illness and other factors influencing antibiotic use. We utilised a before-and-after design [27] with antibiotic usage and adequacy of antibiotic coverage (as mismatches) as the key processes that were most likely to be targeted by the intervention. We used logistic regression with adjustment for other risk factors to demonstrate a significant change in the proportion of patients commenced on each antibiotic.

The second major limitation is the lack of detailed clinical data that would provide further information about the adequacy of prescribing. Although we recorded the presumed indication for commencing antibiotic therapy, collection of detailed clinical information and other tests such as radiology was beyond the scope of the study. To avoid potential influence on prescribing patterns, we did not consult the treating clinicians. In evaluating antibiotic coverage, the analysis included isolates that could have been contaminants rather than pathogens. Similarly, the use of broad-spectrum antibiotics may be clinically appropriate in some clinical situations despite the antibiotic susceptibility profile of identified isolates. The study itself may have influenced prescribing to an unknown degree for any clinicians who became aware that their behaviour was being monitored.

Computerised-assisted decision support will become an important facet of antibiotic stewardship in the twenty-first century as medical decision support and hospital information systems become more sophisticated. The current best systems use is computerised physician order entry with advanced decision support as exemplified by the Intermountain Healthcare

group [11]. However, computerised physician order entry remains very uncommon, largely due to the high cost of implementation and the challenges to get physicians to use these programs [18]. Antibiotic decision support provided by tools such as ADVISE, pharmacy based [15, 16, 28] or web-based systems [29] have the potential to be much more cost effective due to the lower development costs, less integration requirements and easier implementation.

We have demonstrated the successful integration of an antibiotic decision support tool into a busy intensive care unit. The introduction of ADVISE was accompanied by physician acceptance and enthusiasm, and led to measurable improvements in antibiotic use. We believe that strong clinician support, the provision of collated microbiology reports and real-time decision support at the point of care were the key factors for the success of this pilot project [30].

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Table 1: Baseline characteristics of study population

Characteristic	Pre intervention (N=524)	Intervention (N=536)
Age, years (mean)	58±19.1	59±19.4
Gender, n (%)		
Male	316 (60)	323 (60)
Unit, n(%)		
Surgical	288 (55)	296 (55)
Medical	236 (45)	240 (45)
APACHE II score (mean)	13.8± 6.9	16.4±7.8
Patients intubated, n (%)	312 (60)	311 (60)
Antibiotics used, n (%)	346 (66)	363 (68)
Reason for initiation of antibiotics*		
Suspected infection, n (%)	254 (73)	287 (79)
Documented infection, n (%)	22 (6)	14 (4)
Surgical prophylaxis, n (%)	67 (19)	62 (17)
Positive microbiology, n (%)	107 (20)	79 (15)
Readmission	35 (7)	39 (7)
30-day mortality, n (%)	100 (19)	106 (19.8)

± sign indicates standard deviation

*unavailable for 3 patients

Table 2: Unadjusted odds ratios comparing the proportion of patients prescribed antibiotics in the pre-intervention and intervention groups

	Proportion of patients treated (%)		Odds ratio	95% CI	p value
	Pre-intervention	Intervention			
	3 rd generation cephalosporins	39.1			
Carbapenems	13.4	10.3	0.74	[0.51, 1.08]	0.12
Vancomycin	22.1	19.4	0.84	[0.63, 1.13]	0.27
Metronidazole	23.3	21.2	0.86	[0.62, 1.19]	0.37
1 st generation cephalosporins	19.8	20.7	1.02	[0.88-1.18]	0.72
Penicillins*	16.2	15.3	0.93	[0.67, 1.29]	0.68
Gentamicin	7.0	7.2	1.17	[0.70, 1.96]	0.54
Extended spectrum penicillins**	3.4	5.0	1.49	[0.81, 2.74]	0.20
Ciprofloxacin	4.2	6.0	1.45	[0.83, 2.53]	0.19
Macrolides	10.4	17.9	1.83	[1.27, 2.64]	0.001

*Includes benzylpenicillin, amoxicillin, flucloxacillin

**Includes ticarcillin/clavulanate and piperacillin/tazobactam

Table 3: Unadjusted odds ratios (OR) for factors influencing the proportion of patients prescribed ceftriaxone, vancomycin and carbapenems

	Ceftriaxone			Vancomycin			Carbapenems		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Intervention	0.72	[0.56, 0.93]	0.01	0.85	[0.63, 1.14]	0.27	0.74	[0.51, 1.08]	0.12
Apache II score	1.03	[1.01, 1.05]	<0.001	1.09	[1.08, 1.12]	<0.001	1.08	[1.05, 1.10]	<0.001
Infection	16.44	[11.35, 23.81]	<0.001	20.22	[11.36, 36.00]	<0.001	20.66	[9.00, 47.37]	<0.001
Pos microbiology	2.75	[1.98, 3.79]	<0.001	10.05	[7.05, 14.32]	<0.001	7.28	[4.88, 10.87]	<0.001
Sex	0.87	[0.67, 1.12]	0.29	1.14	[0.84, 1.55]	0.41	0.88	[0.61, 1.29]	0.52
Readmission	1.19	[0.73, 1.94]	0.48	3.05	[1.87, 4.95]	<0.001	2.64	[1.49, 4.66]	0.001
Died in ICU	1.73	[1.18, 2.54]	0.01	2.44	[1.62, 3.67]	<0.001	3.17	[2.00, 5.03]	<0.001
Log LOS**	1.87	[1.64, 2.14]	<0.001	3.49	[2.90, 4.21]	<0.001	3.27	[2.64, 4.05]	<0.001
Medical patient	2.28	[1.76, 2.94]	<0.001	1.08	[0.80, 1.46]	0.60	1.00	[0.69, 1.46]	1.00
Intubation	2.10	[1.61, 2.75]	<0.001	2.54	[1.81, 3.57]	<0.001	2.70	[1.72, 4.22]	<0.001

Log LOS - Log transformed length of stay, Infection - Suspected infection

Table 4: Final adjusted model showing a reduction in the proportion of patients prescribed ceftriaxone, vancomycin and carbapenems in the intervention group.

	Ceftriaxone			Vancomycin			Carbapenems		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Intervention	0.58	[0.42, 0.79]	0.001	0.67	[0.45, 1.00]	0.05	0.61	[0.39, 0.97]	0.04
Apache II score	0.98	[0.96, 1.00]	0.20	1.08	[1.05, 1.10]	<0.001	1.05	[1.02, 1.08]	0.003
Intubation	1.16	[0.81, 1.68]	0.41	0.65	[0.41, 1.05]	0.08	0.69	[0.39, 1.23]	0.21
Infection	15.36	[10.05, 23.48]	<0.001	8.83	[4.52, 17.23]	<0.001	7.71	[2.97, 20.00]	<0.001
Pos microbiology	0.73	[0.46, 1.16]	0.18	1.93	[1.19, 3.13]	0.01	1.25	[0.73, 2.14]	0.41
Readmission	0.82	[0.46, 1.45]	0.49	3.04	[1.59, 5.80]	0.001	2.32	[1.15, 4.68]	0.02
Died in ICU	1.16	[0.70, 1.91]	0.20	1.46	[0.83, 2.55]	0.18	2.35	[1.30, 4.27]	0.005
Log LOS	1.28	[1.04, 1.58]	0.02	2.23	[1.73, 2.88]	<0.001	2.50	[1.87, 3.34]	<0.001
Medical patient	2.22	[1.62, 3.06]	<0.001	0.91	[0.41, 1.05]	0.63	0.79	[0.39, 1.23]	0.57

Log LOS – log transformed length of stay

Table 5: Timeliness and Adequacy of Antibiotic Therapy for all Isolates*

Antibiotic Management	Pre- intervention N (%)	Intervention N(%)	Odds Ratio	95% CI	p value
Untreated isolates	22/303 (7.3)	12/237 (5.1)	0.69	[0.35, 1.37]	0.20
Delayed therapy	40/278 (14.4)	36/225 (16.0)	1.12	[0.73, 1.68]	0.62
Initial susceptibility mismatch**	48/197 (24.4)	23/151 (15.2)	0.63	[0.39, 0.98]	0.02
Directed susceptibility mismatch	41/240 (17.1)	30/185 (16.2)	0.94	[0.61, 1.45)	0.90
Antibiotic spectrum reduced after susceptibilities available	14/185 (7.0)	24/155 (15.6)	2.20	[1.17 , 4.11]	0.01

*The proportion of sterile isolates was 20% and 19% in the pre-intervention and intervention groups respectively. There was no significant difference between sterile and non-sterile isolates

** For isolates where antibiotics were commenced *after* identification of the organism