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## Original Article

# THE IMPACT OF AN ANTIMICROBIAL STEWARDSHIP INTERVENTION IN NEONATAL INTENSIVE CARE – RECOMMENDATIONS AND IMPLEMENTATION

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**Keywords:** antimicrobial stewardship, antibiotic resistance, neonates

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**Conflicts of interest:** The authors have no conflicts of interest to disclose.

**Brief Points:**

**What is already known on this topic**

1. Neonatal intensive care units have among the highest rates of antimicrobial resistance worldwide, predominantly driven by high antibiotic use.
2. Despite this, evidence for Antimicrobial Stewardship interventions in this setting is limited.

**What this paper adds**

1. A collaborative audit-feedback Antimicrobial Stewardship intervention significantly improved antimicrobial prescribing practices in neonatal intensive care.

2. The intervention was effective in identifying inappropriate antimicrobial prescribing and facilitating implementation of recommendations to optimise prescribing practices using existing resources.

### **Abstract**

**Aims:** To (i) determine the appropriateness of antimicrobial prescribing in the Neonatal Intensive Care Unit (NICU) and (ii) assess the impact of a collaborative Antimicrobial Stewardship (AMS) intervention on prescribing practices.

**Methods:** The intervention was a weekly AMS audit-feedback joint ward round (6-month period) of Neonatology and Infectious Diseases clinicians in a tertiary NICU in Melbourne, Australia. Antibiotic prescriptions were audited and recommendations delivered in real-time. The proportion of recommendations implemented was used to assess acceptability of the intervention.

**Results:** During the study period there were 23 AMS rounds, during which 249 patients were reviewed at 627 separate episodes. Of these, 233 (37%) episodes were for patients receiving antimicrobials. Of these, 147 (63%) received empirical antimicrobial treatment, 43 (18%) targeted antimicrobial treatment, and 43 (18%) antimicrobial prophylaxis. There were 58/233 (25%) episodes of inappropriate antibiotic use, and 62 recommendations for improvement. Most common recommendations were to narrow (33/62, 53%) or stop (12/62, 19%) antimicrobials. The majority (45, 73%) of recommendations were accepted, resulting in significant improvement in the proportion of the 233 episodes that had completely appropriate antibiotic prescribing: 175 (75%) to 217 (93%) (RR 1.2, 95%CI 1.1-1.3 p<0.001).

**Conclusions:** A collaborative audit-feedback AMS intervention was effective in identifying inappropriate antimicrobial prescriptions and impacted positively on treatment plans.

Ancillary benefits were improved communication between departments and the revision of antimicrobial prescribing guidelines.

**Keywords:** antimicrobial stewardship, antibiotic resistance, neonates

## Introduction

Infants in neonatal intensive care units (NICU) constitute a population with among the highest rates of antimicrobial resistance (AMR) worldwide.<sup>1</sup> Antimicrobial use is a key driver of AMR, and antibiotics are the most frequently prescribed medicines in the NICU.<sup>2,3</sup> Moreover, up to half of antimicrobial agents prescribed in hospitals may be inappropriate.<sup>4</sup> Inappropriate antimicrobial use has been directly associated with adverse outcomes in NICU including the emergence of extensively drug resistant organisms and increased rates of fungaemia, necrotising enterocolitis and death.<sup>5,6</sup>

Antimicrobial stewardship (AMS) programs ideally provide multidisciplinary (e.g. infectious diseases (ID), microbiology, pharmacy) interventions designed to ensure that the right antibiotic is prescribed at the right dose for the right duration. The ‘appropriateness’ of antimicrobial prescriptions describes the optimal therapeutic use of antibiotics, although various definitions exist based on the *in vitro* susceptibilities of bacteria, clinical practice guidelines, or ID/AMS team opinion.<sup>7,8</sup> Ancillary benefits of AMS programs include education and information dissemination which support professionals to reduce unnecessary antibiotic use.<sup>9</sup> AMS strategies include prescriber audit-feedback, formulary restriction and prior authorisation.<sup>10</sup> Audit-feedback interventions involve a review of antibiotic prescriptions with feedback given to the prescribers in real-time, which facilitates discussion of recommendations. Audit-feedback strategies have been shown to improve antibiotic prescribing practices in general paediatric wards.<sup>11</sup> There is clearly a need for effective AMS strategies to minimise the risk of AMR associated with inappropriate use of antimicrobials in NICU, yet prospective studies assessing AMS interventions in the NICU are lacking.<sup>12,13</sup>

This study describes the implementation of a weekly audit-feedback intervention in a NICU. The study objectives were (i) to determine the appropriateness of antimicrobial prescribing in NICU and (ii) to assess the acceptance and impact of a collaborative AMS audit-feedback intervention on prescribing practice.

## Methods

*Design and setting:* This was a prospective study in the NICU at the Royal Children's Hospital (RCH) Melbourne over six months, from 6<sup>th</sup> October 2014 to 31<sup>st</sup> March 2015. The RCH NICU is a tertiary referral unit providing care for neonates with complex medical and surgical conditions. It accepts ex-utero transfers from the state of Victoria, interstate and overseas, as well as admissions from the RCH Emergency Department, with approximately 650 admissions per year.

*Participants:* All NICU inpatients were reviewed, with a particular focus on those receiving intravenous or oral antibacterials, antivirals or antifungals.

*Data collection:* De-identified data collected prior to, during and post the AMS round were entered prospectively into a REDCap (Research Electronic Data Capture) database developed for the study.<sup>14</sup> Data were collected on demographics, primary indication for admission, respiratory and circulatory support at time of review, indication for antibiotics, current antibiotic prescriptions (excluding oral/topical nystatin prophylaxis), appropriateness of antibiotic regimens, and AMS recommendations made and implemented. Antibiotic regimens were defined as empirical (for suspected infection from a presumed or unknown source), targeted (if based on positive culture or molecular tests), or prophylactic.

*Intervention:* A collaborative audit-feedback NICU AMS round was introduced, with audit of the appropriateness of antibiotic prescriptions, followed by feedback of recommendations to make changes where applicable. The weekly AMS round was attended by senior NICU medical staff (consultant neonatologist on ward duty and NICU fellow) and the paediatric ID fellow(s). The AMS round was held in the NICU (duration 30-60 min). All current inpatients were discussed and antimicrobial prescriptions were reviewed in the context of the clinical information presented by the neonatal team, available laboratory tests and relevant medical imaging.

*Outcomes:* The main outcomes were appropriateness of antibiotics and the acceptance of recommended changes for inappropriate prescriptions. The appropriateness of an antimicrobial prescription was determined during the AMS round by the ID fellow, a doctor usually in the final year of their professional ID training. The decision was based on the clinical scenario, hospital antibiotic policy and microbiological results (when available). Inappropriate antimicrobial prescriptions were categorised using published standardised terminology as (i) an inappropriate decision (the prescription of antibiotics when none are

needed, or not being on antibiotics when they are indicated), (ii) an inappropriate choice (incorrect antibiotic for the clinical scenario, including those considered too narrow, too broad or redundant antimicrobials, or (iii) inappropriate application (incorrect dose, interval, route or duration).<sup>15</sup> The ID fellow considered the appropriateness of a prescription and made recommendations in real time, which included (i) stop all antimicrobials, (ii) narrow/broaden antimicrobial spectrum, or (iii) change antimicrobial dose or duration. Multiple recommendations could be made per review. A chart review of antimicrobial prescriptions was undertaken 24-hours after the AMS round to assess the implementation of recommendations.

*Statistical analysis:* Data were analysed using Stata statistical software version 14.0 (StataCorp). Fisher Exact test was used to analyse categorical variables and t test was used for continuous variables. Comparisons are described by relative risk (RR) with 95% confidence intervals (CI), and  $p < 0.05$  was considered significant.

*Ethics:* Ethical approval for the study was obtained from the RCH Human Research Ethics Committee (HREC35074A).

## Results

Over the 6-month study period, there were 23 weekly AMS rounds, with 249 infants assessed at 627 review episodes. All neonates in this tertiary unit are outborn, with 224 (90%) admitted as interhospital transfers and 10% admitted from the Emergency Department. The majority of infants (162, 65%) were  $>37$  weeks gestation although the lowest gestation was 24 weeks (median 38 weeks) (Table 1). Birthweight ranged from 591-5102 grams and 116 (47%) were female. 65 (26%) infants were receiving invasive ventilation during at least one review episode, and 20 (8%) inotropic support. Patients were more likely to receive antibiotics than not if they were receiving invasive ventilation (RR 6.3, 95%CI 3.0-13.0,  $p < 0.001$ ) or inotropic support (RR 14.8, 95%CI 1.4-16.8,  $p = 0.006$ ) during at least one episode (Table 1). No other factors differentiated whether infants received antibiotics.

### *Antimicrobial usage in the NICU*

The proportion of infants on antimicrobials at each AMS round ranged from 6/31 (19%) to 16/27 (59%), median 37% (Figure 1). Of the 627 review episodes, 233 (37%) were for

patients receiving antimicrobials. In 147 (63%) of these 233 antimicrobial episodes, the antibiotic treatment was empirical (organism not identified): 111 (48%) for an unknown source, and 36 (15%) for a presumed source based on symptoms and signs including temperature instability and respiratory deterioration. Empirical antibiotics were most commonly used to treat suspected infections, most commonly meningitis (14 episodes, 6%) and lower respiratory tract infection (11, 5%) (Figure 2). Targeted treatment (organism identified) accounted for 43 (18%) episodes, most commonly urinary tract infection (UTI) (10 episodes, 4%), meningitis (9, 4%) and bacteraemia (9, 4%). The remainder of antibiotic episodes were for prophylaxis: 43 (18%) episodes, most commonly risk of UTI (26 episodes, 60%), perioperative prophylaxis (15, 35%) and immunosuppression (2, 5%).

There were 468 prescriptions for antimicrobials, 408 (87%) for treatment and 60 (13%) for prophylaxis. Patients received a minimum of 1 and maximum of 4 antimicrobials per episode, (median 2). Of the 408 antimicrobials for treatment, 390 (96%) were antibacterials, 14 (3%) antivirals and 4 (1%) antifungals. Twenty different antimicrobial drugs accounted for all treatment prescriptions (Table 2). The DU50 (number of drugs used for the top 50% of usage when ranked by frequency of prescription) was 3 antibiotics (benzylpenicillin, gentamicin and cefotaxime) and the DU90 was 7. Seven different antibiotics were used for perioperative prophylaxis (Table 3).

#### *Appropriateness of antimicrobial prescribing*

There were no episodes where a patient was not receiving antimicrobials who was judged to need them. Of the 233 reviews of patients on antimicrobials, 175 (75%) were deemed to be receiving a completely appropriate regimen, with the remaining 58 (25%) having at least one inappropriate antimicrobial prescription. Episodes with at least one inappropriate prescription included: 11 (19%) episodes with an inappropriate decision to prescribe antimicrobials (i.e. no antimicrobial required), 43 (74%) inappropriate choice (too broad or too narrow), and 4 (7%) inappropriate application (dose or duration) (Table 4). Use of antibiotics was deemed inappropriate in 39/147 (27%) empirical episodes versus 15/43 (35%) for targeted treatment (RR 0.8, 95%CI 0.5-1.2 p=0.2). Inappropriate choice was less likely for empirical treatment: 26 (18%) versus 14 (33%) (RR 0.5, 95%CI 0.3-0.95, p=0.03). All 4 episodes of inappropriate use of antimicrobials for prophylaxis were for perioperative prophylaxis.

### *Implementation of recommendations*

Sixty-two individual recommendations were made for the 58 patient episodes with inappropriate prescriptions identified at AMS rounds, as for some reviews more than one recommendation was made, e.g. change dose and duration (Table 4). The most common recommendations made were to narrow (33 recommendations, 53%) or stop (12, 19%) antimicrobials. No recommendations were made to change route or interval of administration, as there was no inappropriateness in these areas.

The majority (45, 73%) of these recommendations were accepted by NICU senior medical staff (Table 4). Recommendations most likely to be implemented were to stop all antimicrobials (11/12, 92% accepted). There was no difference between implementation of recommendations to narrow antimicrobial spectrum (24/33, 73%) and broaden spectrum (5/7, 71%) (RR 1.0, 95%CI 0.6-1.7 p=0.6). Overall, implementation of recommendations improved the proportion of episodes with completely appropriate antibiotic prescribing from 175 (75%) to 217 (93%) (RR 1.2, 95%CI 1.1-1.3 p<0.001).

Additional advice was given during the AMS rounds for 96 (41%) of the 233 reviews of patients on antimicrobials: planning duration (62 episodes, 27%), additional investigations (16, 7%), interpretation of investigations (7, 3%), formal consult to ID service (6, 3%), antimicrobial plan in case of imminent deterioration (3, 1%) and provision of new microbiological data not known to the treating team (2, 1%).

No detrimental impact was detected on patient outcomes, with respect to frequency of bacteraemia, antimicrobial resistance, length of stay and mortality, following implementation of the AMS intervention (Table 5). Mortality was similar in the 6 months before (20/364, 5%), during (13/331, 4%) and after (15/385, 4%) the study period.

### **Discussion**

This study found that a collaborative AMS intervention using existing personnel resource, in a NICU providing care for neonates with complex medical and surgical conditions, was useful, acceptable and significantly improved the proportion of infants on appropriate antibiotic regimens.

The proportion of neonates on antibiotics (37%, range 19%-59%) at each AMS round is comparable to local and international data. A single-day point prevalence survey in Australian hospitals found the proportion of patients receiving antimicrobials across six NICUs was 28% (range 15%-42%).<sup>7</sup> A worldwide point prevalence survey including 240 NICUs reported an overall rate of 30% on antimicrobials with a wide range between countries.<sup>16</sup> The two most commonly prescribed antimicrobials for treatment reflect the institutional NICU guidelines for empirical treatment of early-onset sepsis (benzylpenicillin and gentamicin), and are comparable to the most commonly prescribed antibiotics in neonates within Australia, Northern Europe and Africa.<sup>16</sup> Broad-spectrum antimicrobials such as meropenem and piperacillin-tazobactam were rarely used. Our institutional NICU rates of resistance to broad-spectrum antibiotics are low with resistance to Gram-negative bacteria currently 8% for cefotaxime, and 0% for piperacillin-tazobactam and meropenem. This is both a result of and has an impact on low rates of broad-spectrum prescribing.

A quarter of all episodes were deemed to have inappropriate antimicrobial prescriptions. This is comparable to a study in 4 NICUs in the United States that showed 28% of antibiotic courses were inappropriate.<sup>17</sup> The investigators concluded that AMS efforts should focus on narrowing or de-escalating therapy and instituting protocols to limit prophylaxis. However, the study was retrospective and did not assess the impact of an intervention. Almost three-quarters of recommendations made during AMS rounds were implemented by NICU medical staff, most commonly to narrow or stop antimicrobials. This is a critical outcome in concluding that the AMS round is both useful (inappropriate prescribing is identified) and acceptable (inappropriate prescribing is rectified). The results compare favourably with another study of interdisciplinary rounds involving infectious disease specialists in adult ICU, showing acceptance of 66% of recommendations.<sup>18</sup> The high uptake of recommendations in the present study may be explained by the collaborative nature of the AMS rounds. The participation of a senior neonatologist on ward duty was essential in influencing

antimicrobial prescriptions, allowing discussions of the nuances of specific scenarios and enhancing mutual understanding between the ID and neonatology teams. This regular AMS intervention additionally served as a catalyst for the collaborative development between ID/AMS and neonatal teams of comprehensive antibiotic guidelines (beyond early-onset and late-onset sepsis), with choices, recommended duration and risk factors to consider for specific infections (Supporting Information: appendix 1). Clinical guidelines in themselves can form part of an effective AMS strategy,<sup>19</sup> although considerable variation exists in antibiotic guidelines between similar neonatal units due to lack of consensus.<sup>20,21</sup> Since the completion of this study, AMS rounds have become more efficient with the change from paper to electronic prescribing, enabling rapid changes in prescriptions during the round. AMS rounds could be further improved with a dedicated clinical pharmacist.<sup>22</sup>

AMS is a balance between ensuring that sufficient antibiotics are prescribed to be safe, while limiting excessive use. In the longer term, a principal goal of AMS is to slow the increase of AMR, and the timeframe of our study is too short to show this. However, the absence of worsening clinical outcomes due to reducing antibiotic use is an important measure. Therefore, it is reassuring that rates of bacteraemia, length of stay and mortality all remained low during the AMS study period with no signal of any increase, and that there was no rebound in the six months afterwards.

Study limitations include this being a single centre study, which may limit the external applicability of the results to NICUs similar to RCH NICU with regards to size (large), care structure (tertiary) and patient mix (a high proportion of complex patients). However, if this type of relatively simple intervention is acceptable and effective in this highly specialised setting, there is reason to be optimistic that it would work in a less intense setting.

Appropriateness data was captured for antimicrobial regimens as a whole, as opposed to individual antimicrobial prescriptions, so may not reflect the complexity of individual prescriptions, although the message is unlikely to be different. In addition, while appropriateness was determined based on the clinical scenario presented by the neonatal team and using microbiology results when available, clinical judgement is by its nature subjective. The cross-sectional nature of the reviews meant that inappropriate duration was frequently not captured, a previously identified problem with perioperative antibiotics in particular.<sup>7,23</sup>

This highlights the need for evidence-based guidelines to prevent infants from receiving unnecessary prolonged prophylaxis, which may increase the risk of AMR.<sup>24</sup> We did not capture whether lack of implementation of recommendations was due to disagreement with the decision or suboptimal communication with NICU ward staff not present during rounds.

Despite the frequency of inappropriate prescribing, the AMS rounds provided an effective intervention (identification, recommendation and facilitation of successful implementation) in significantly improving antimicrobial prescribing practices in the NICU. We identified areas for improvement, confirming the need for targeted real-time AMS strategies in the NICU. The time commitment required was low for the success of this intervention, making it attractive to busy teams. To assist in the case for additional AMS resources to expand this activity, an economic analysis would be useful, both of antimicrobials used and of complications of inappropriate use of antimicrobials. The improved engagement between the NICU and ID teams around antibiotic use resulting from this intervention led directly to the collaborative development of a specific neonatal antibiotic guideline for empirical and targeted antibiotic prescribing.

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**Table legends**

**Table 1.** Demographics and clinical features of patients assessed during AMS rounds

**Table 2.** Antimicrobials used for treatment

**Table 3.** Antimicrobials used for prophylaxis

**Table 4.** Appropriateness and acceptance of AMS recommendations

**Table 5.** Patient outcomes in the 6 months before, during and after the study period

**Table 1.** Demographics and clinical features of patients assessed during AMS rounds

Characteristics		Total patients n=249 (%)	Patients receiving antibiotics during at least one episode n=141 (%)	Patients not receiving antibiotics during any episode n=108 (%)	RR (95% CI) p value
Sex	Female	116 (47%)	72 (51%)	44 (41%)	1.5 (0.9-2.5) 0.07
Gestational age (weeks)	<25	4 (2%)	2 (1%)	2 (2%)	0.8 (0.1-5.5) 0.6
	25 - 29+6	10 (4%)	7 (5%)	3 (3%)	1.8 (0.5-7.2) 0.3
	30 - 34+6	45 (18%)	32 (23%)	13 (12%)	1.3 (0.8-1.9) 0.2
	35 - 36+6	28 (11%)	18 (13%)	10 (41%)	1.1 (0.7-2.0) 0.4
	≥ 37	162 (65%)	82 (58%)	4 (41%)	0.9 (0.8-1.1) 0.2
Birth weight (g)	<1000	13 (5%)	8 (6%)	5 (5%)	1.2 (0.4-3.9) 0.5
	1000-1499	10 (4%)	7 (5%)	3 (3%)	1.8 (0.5-7.2) 0.3
	1500-2499	55 (22%)	33 (23%)	22 (20%)	1.2 (0.6-2.2) 0.3
	≥ 2500	171 (68%)	93 (66%)	78 (72%)	0.7 (0.4-1.3) 0.2
Respiratory support <sup>†</sup>	Invasive ventilation	65 (26%)	55 (39%)	10 (9%)	6.3 (3.0-13.0) <0.001
Circulatory support <sup>†</sup>	Inotropes	20 (8%)	17 (12%)	3 (3%)	14.8 (1.4-16.8) 0.006
Primary indication for admission	Hospital transfer - medical	124 (50%)	71 (50%)	53 (49%)	1.0 (0.6-1.7) 0.5
	Hospital transfer - surgical	100 (40%)	56 (40%)	44 (41%)	1.0 (0.6-1.6) 0.5
	From community - medical	24 (10%)	13 (9%)	11 (10%)	0.9 (0.4-2.1) 0.5
	From community - surgical	1 (0.4%)	1 (1%)	0 (0%)	N/A 0.6

<sup>†</sup>Patients receiving respiratory/circulatory support during at least one review episode.

**Table 2.** Antimicrobials used for treatment

<b>Antimicrobial</b>	<b>No. (%) of prescriptions (n=408)</b>	
Gentamicin	119 (29%)	
Benzympenicillin	65 (16%)	
Cefotaxime	64 (16%)	DU50
Vancomycin	54 (13%)	
Metronidazole	38 (9%)	
Flucloxacillin	25 (6%)	
Aciclovir	14 (3%)	DU90
Amoxicillin	6 (1.5%)	
Fluconazole	4 (1%)	
Ticarcillin-clavulanate	3 (0.7%)	
Amikacin	2 (0.5%)	
Piperacillin-Tazobactam	2 (0.5%)	
Meropenem	2 (0.5%)	
Ciprofloxacin	2 (0.5%)	
Ceftazidime	1 (0.2%)	
Cephazolin	1 (0.2%)	
Clindamycin (oral)	2 (0.5%)	
Trimethoprim-sulfamethoxazole (oral)	2 (0.5%)	
Trimethoprim (oral)	1 (0.2%)	
Amoxicillin-clavulanate (oral)	1 (0.2%)	

All antimicrobials were administered via intravenous route, unless otherwise specified via oral route.

DU50 and DU90 = antimicrobials used for the top 50% and 90% of usage, respectively.

**Table 3.** Antimicrobials used for prophylaxis

<b>Antimicrobial</b>	<b>No. (%) of prescriptions (n=60)</b>	
Trimethoprim (oral)	24 (40%)	
Gentamicin	11 (18%)	
Vancomycin	7 (12%)	DU50
Benzylpenicillin	4 (7%)	
Cefotaxime	3 (5%)	
Metronidazole	3 (5%)	
Cefazolin	3 (5%)	DU90
Fluconazole (oral)	2 (3%)	
Trimethoprim-sulfamethoxazole (oral)	2 (3%)	
Flucloxacillin	1 (2%)	

All antimicrobials were administered via intravenous route, unless otherwise specified via oral route.

DU50 and DU90 = antimicrobials used for the top 50% and 90% of usage, respectively.

**Table 4.** Appropriateness and acceptance of AMS recommendations

Episodes	Type of AMS recommendation	Recommendation made	Change made within 24h	Change not made within 24h	RR (95% CI) p value
No. (%) n=233		No. (% of total) n=62	No. (%) n=45	No. (%) n=17	
Appropriate					
175 (75%)					
Inappropriate decision	Stop all antimicrobials	12 (19)	11 (24)	1 (6)	5.2 (0.6-44) 0.09
11 (5%)					
Inappropriate choice	Narrow antimicrobial spectrum	33 (53)	24 (53)	9 (53)	1.0 (0.3-3.1) 0.6
	Broaden antimicrobial spectrum	7 (11)	5 (11)	2 (12)	0.9 (0.2-5.4) 0.6
	Change antimicrobial for site specific indication	5 (8)	3 (7)	2 (12)	0.5 (0.1-3.4) 0.4
43 (18%)					
Inappropriate application	Change dose of antimicrobial	2 (3)	1 (2)	1 (6)	0.4 (0.0-6.2) 0.4
	Lengthen planned duration	2 (3)	1 (2)	1 (6)	0.4 (0.0-6.2) 0.4
	Shorten planned duration	1 (2)	0 (0)	1 (6)	NA 0.3
4 (2%)					

**Table 5.** Patient outcomes in the 6 months before, during and after the study period

	Pre-study	During study	Post-study
New positive blood culture <sup>†</sup> /total (%)	38/297 (13)	21/268 (8)	24/246 (10)
Coagulase negative staphylococci (CoNS)	31	13	20
<i>Staphylococcus aureus</i>	1	0	1
<i>Esherischia coli</i>	1	1	1
Group B streptococci	0	0	0
Other Gram positive bacteria	2	3	1
Other Gram negative bacteria	2	3	1
<i>Candida</i> species	1	1	0
Antimicrobial resistance			
Methicillin-resistant <i>S. aureus</i>	0/1	0/0	0/1
Vancomycin-resistant <i>Enterococcus</i> species	0/0	0/0	0/1
Cefotaxime-resistant Enterobacteriaceae <sup>‡</sup>	1/3	0/3	1/2
Gentamicin-resistant Enterobacteriaceae <sup>‡</sup>	0/3	0/3	0/2
Length of stay, median days per admission	6	6.5	6
Mortality, no. deaths/total no. patients (%)	20/364 (5)	13/331 (4)	15/385 (4)

<sup>†</sup>Excludes subsequent cultures with same organism within 14 days

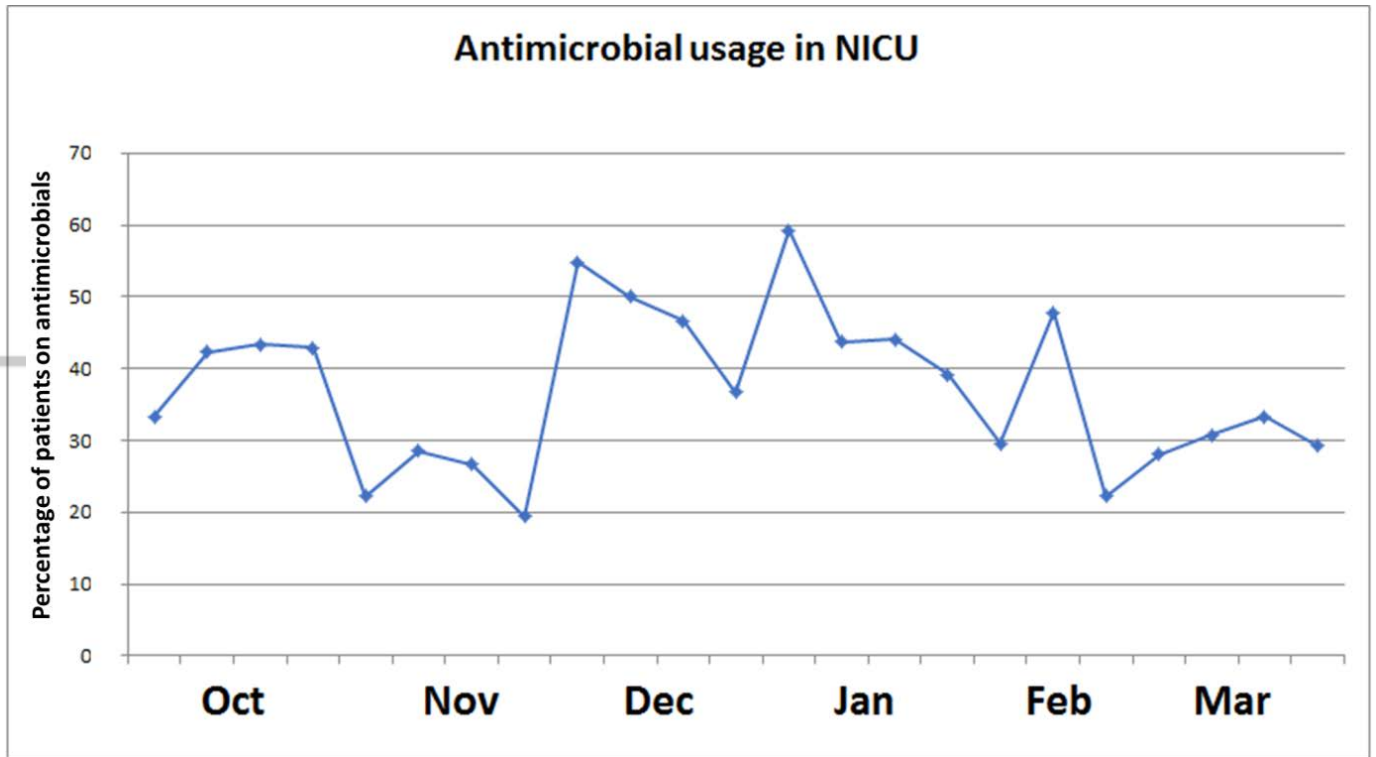
<sup>‡</sup>Excludes *Pseudomonas* species

## **Figure legends**

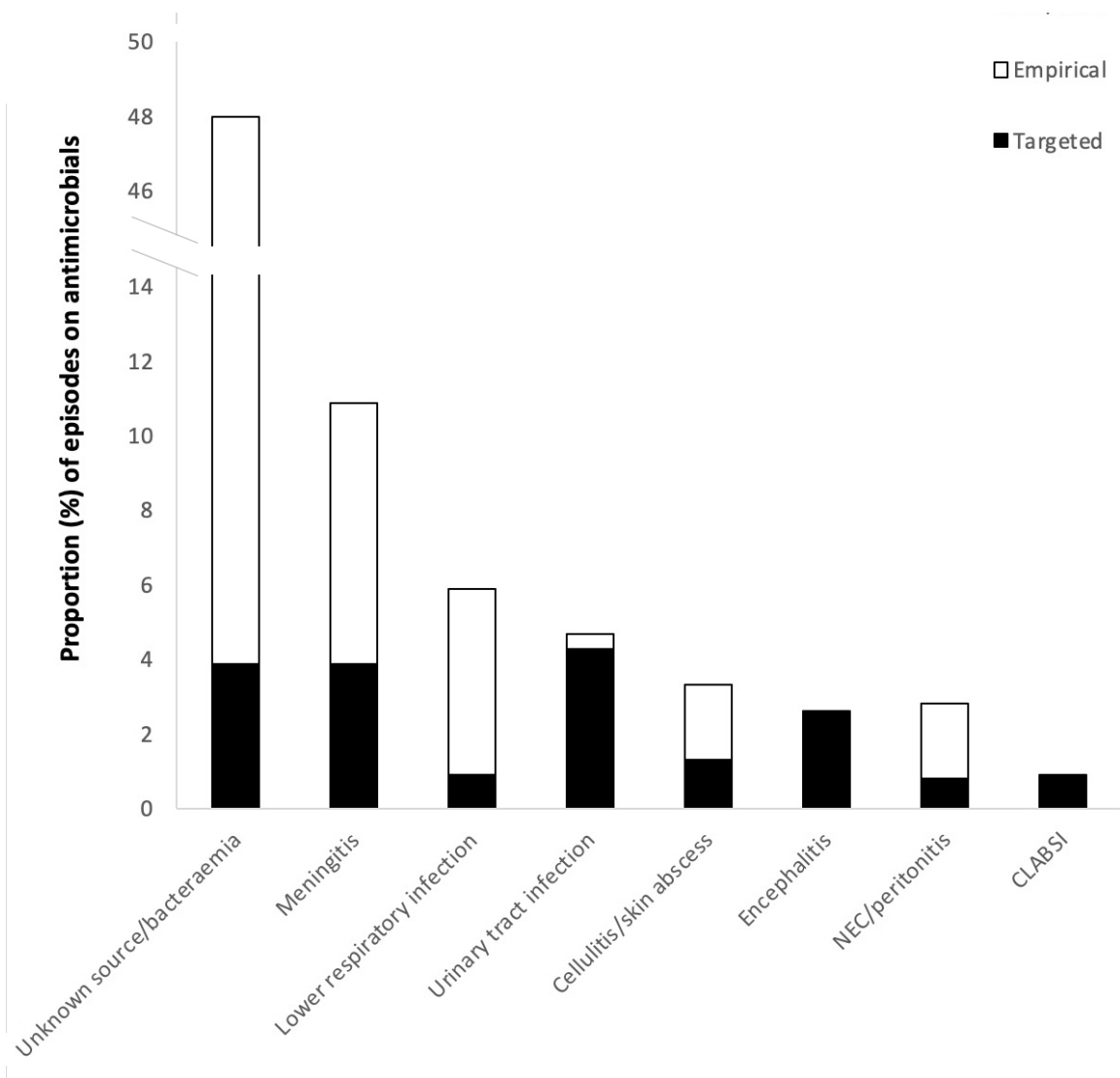
**Figure 1.** Proportion of patients receiving antimicrobials at each AMS round, Oct 2014-March 2015

**Figure 2.** Indications for antimicrobial treatment.

Abbreviations: UTI, urinary tract infection; LRTI, lower respiratory tract infection; NEC, necrotising enterocolitis; CLABSI, central line-associated blood stream infection.



**Figure 1.** Percentage of patients receiving antimicrobials at each AMS round, Royal Children’s Hospital NICU, Melbourne, Oct 2014-March 2015



**Figure 2.** Indications for antimicrobial treatment

Abbreviations: NEC, necrotising enterocolitis; CLABSI, central line-associated blood stream infection.

## Original Article

# THE IMPACT OF AN ANTIMICROBIAL STEWARDSHIP INTERVENTION IN NEONATAL INTENSIVE CARE – RECOMMENDATIONS AND IMPLEMENTATION

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**Keywords:** antimicrobial stewardship, antibiotic resistance, neonates

**Running head title:** *Antimicrobial stewardship in the NICU*

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**Conflicts of interest:** The authors have no conflicts of interest to disclose.

**Brief Points:**

**What is already known on this topic**

1. Neonatal intensive care units have among the highest rates of antimicrobial resistance worldwide, predominantly driven by high antibiotic use.
2. Despite this, evidence for Antimicrobial Stewardship interventions in this setting is limited.

**What this paper adds**

1. A collaborative audit-feedback Antimicrobial Stewardship intervention significantly improved antimicrobial prescribing practices in neonatal intensive care.
2. The intervention was effective in identifying inappropriate antimicrobial prescribing and facilitating implementation of recommendations to optimise prescribing practices using existing resources.