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Short Communication

# Selective antibiotic susceptibility reporting and broad-spectrum intravenous antibiotic use: A multicentre ecological study

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ABSTRACT

Recent estimates of inpatient antibiotic use in the USA suggest that broad-spectrum antibiotic use has increased significantly. The objective of this study was to assess the impact of a selective antibiotic susceptibility reporting intervention on broad-spectrum intravenous (i.v.) antibiotic use in seven hospitals of a health system in New Jersey. This was a retrospective pre- and post-intervention ecological study. Standardised selective antibiotic susceptibility reporting rules were developed and implemented between January 2016 and June 2017. The 8 months before and after each individual hospital's implementation constituted the pre- and post-intervention study periods. The primary outcome was the rate of broad-spectrum i.v. antibiotic use for hospital-onset/multidrug-resistant infections (broad MDR). Secondary outcome measures were the use rates of non-glycopeptide anti-methicillin-resistant *Staphylococcus aureus* (anti-MRSA) agents, carbapenems, non-carbapenem antipseudomonal $\beta$-lactams, third-generation cephalosporins, first/second-generation cephalosporins, fluoroquinolones and narrow-spectrum penicillins. Antibiotic use data were collected as inpatient i.v. antibiotic days of therapy per 1000 patient days (DOT/1000-PD). Interrupted time series analysis with segmented regression was used to compare outcomes. There was no significant change in the use of broad MDR agents (slope change, +0.54 DOT/1000-PD per month, 95% confidence interval −1.78 to 2.87) or other antibiotic classes. Whilst the implementation of selective antibiotic susceptibility reporting across seven hospitals had no impact on overall broad-spectrum i.v. antibiotic use, further study is needed to determine the long-term impact of this intervention.


## 1. Introduction

Antimicrobial resistance is a global public-health concern and strategies to mitigate the development of resistance are urgently needed [1]. Broad-spectrum antibiotic use, in particular, poses an increased risk for the development of antimicrobial resistance [2]. Recent estimates of inpatient antibiotic use in the USA suggest that while overall antibiotic use has not increased, the use of broad-spectrum antibiotics has increased significantly [3]. Close to one-half of all antibiotics prescribed are unnecessary, and those that are prescribed are often broader than required [4]. Selective laboratory antibiotic susceptibility test reporting has been advocated as an antimicrobial stewardship tool to help reduce prescribing of broad-spectrum antibiotic therapy and is recommended by the Infectious Diseases Society of America (IDSA) to promote the use of narrow-spectrum agents when indicated [1]. Despite this recommendation, few data are available regarding the use of this strategy in the USA. A cross-sectional survey of European countries identified that selective antibiotic susceptibility test reporting was not widely implemented (31% based on 36 participating countries) [5]. Some barriers cited included lack of guidelines, system support, resources and professionals' capability.

With the help of our system-wide antimicrobial task force, cascading laboratory antibiotic susceptibility was implemented across several health system campuses. Since this stewardship strategy had not been previously used at these institutions, the setting allowed us to perform a pre- and post-implementation assessment of effectiveness in reducing broad-spectrum antibiotic use. The

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objective of this study was to assess the impact of a selective antibiotic susceptibility reporting intervention on broad-spectrum intravenous (i.v.) antibiotic use in seven hospitals of a health system.

## 2. Methods

This was a retrospective pre- and post-intervention ecological study conducted at seven hospitals within a New Jersey health system. Study hospitals included teaching and non-teaching acute-care facilities with hospital bed sizes varying from 241 to 665. Standardised selective antibiotic susceptibility reporting rules were developed by the health system Antimicrobial Stewardship Committee and were implemented at each site between January 2016 and June 2017. The selective antibiotic susceptibility reporting rules were designed to suppress the susceptibilities of broad-spectrum antibiotic agents for various organisms that were proven susceptible to narrower-spectrum antibiotics. The rules applied primarily to broad-spectrum $\beta$-lactams for susceptible Gram-negative bacteria, and non-glycopeptide anti-methicillin-resistant *Staphylococcus aureus* (anti-MRSA) agents for susceptible Gram-positive bacteria. The complete rules can be found in the Supplementary material. No formal education was provided to prescribers prior to implementation.

The 8 months before and after each individual hospital's implementation constituted the pre- and post-intervention study periods, respectively. Intravenous antibiotic use data were extracted from the electronic medical record and were reported as inpatient antibiotic days of therapy per 1000 patient-days (DOT/1000-PD). Antimicrobial agents were classified according to the US Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) 2017 Antibiotic Use Module definitions [6]. The primary outcome was the rate of broad-spectrum i.v. antibiotic use for hospital-onset or multidrug-resistant infections (antipseudomonal $\beta$-lactams, aminoglycosides, polymyxins and tigecycline; broad MDR). Secondary outcome measures were the use rates of non-glycopeptide anti-MRSA agents, carbapenems, non-carbapenem antipseudomonal $\beta$-lactams, third-generation cephalosporins, first/second-generation cephalosporins, fluoroquinolones and narrow-spectrum penicillins. Interrupted time series analysis with segmented regression was used to compare outcomes. Autoregressive integrated moving average models were generated and analysed using IBM SPSS Statistics v.25.0 (IBM Corp., Armonk, NY). Results were reported as slope changes as well as step changes pre- and post-intervention. Slope changes indicate trends in drug utilisation rates over time, whereas step changes indicate immediate increases or decreases in usage following the intervention.

## 3. Results

A total of 473 352 and 471 888 PDs from the seven hospitals were included in the pre- and post-intervention periods, respectively. There was no significant change in the primary outcome of broad MDR agent use [slope change, +0.54 DOT/1000-PD/month, 95% confidence interval (CI) −1.78 to 2.87; step change, +8.75 DOT/1000-PD, 95% CI −19.03 to 36.52]. The slope change of carbapenem use was −0.77 (95% CI −1.58 to 0.05). The slope change of non-carbapenem antipseudomonal $\beta$-lactams was +1.03 (95% CI −0.59 to 2.66). The associated step change was +11.78 (95% CI −7.69 to 31.24). The slope change of fluoroquinolone use was +0.68 (95% CI −0.08 to 1.45). No significant change in the use of other antibiotic classes was detected. See Table 1 for the complete results.

## 4. Discussion

This interrupted time series analysis evaluating the effect of selective antibiotic susceptibility reporting on antibiotic use across a seven-hospital system found no impact in the 8-month study period. There are several possible explanations for this lack of effect.

One possible explanation is that selective antibiotic susceptibility reporting has no impact on antibiotic prescribing. A review of the literature, however, reveals a variety of studies suggesting a benefit. Coupat et al. [7] and Bourdellon et al. [8] found a selective antibiotic reporting strategy to yield more appropriate antibiotic selection when surveying medical residents with case vignettes. Tan et al. found improved prescribing with this strategy in outpatient settings for urinary tract infection [9]. More recently, Langford et al. evaluated this intervention with respect to a single drug (ciprofloxacin) at a single institution and found a decrease in use and favourable changes in antibiotic susceptibility [10]. Johnson et al. reported increased rates of de-escalation in patients with Gram-negative bacteraemia following implementation of cascade reporting at two hospitals [11]. Another study conducted in Saudi Arabia evaluated the 6-month impact of selective susceptibility reporting across a health system and found dramatic shifts in antibiotic use and institutional susceptibilities for Gram-negative bacterial infections [12]. In summary, existing evidence supports the plausibility of this intervention and demonstrates success particularly when applied in patient- and antibiotic-specific scenarios.

Another possible explanation for the current findings is the lack of formal education provided to prescribers. Co-ordinated education emphasising the purpose of selective antibiotic susceptibility reporting and the value of antibiotic de-escalation could have increased prescriber receptiveness to the intervention. The value of proactive antibiotic stewardship programme (ASP) involvement in realising the benefits of other antibiotic stewardship interventions has been well documented [13]. Whether the same applies to selective antibiotic susceptibility reporting requires further study.

The choice of overall antibiotic use as the outcome evaluated in this study may also explain the lack of benefit with the intervention. Overall antibiotic use was selected because of its value and availability to ASPs for monitoring and goal setting. These results provide insight into how other ASPs might expect a similar intervention to impact an outcome that they are likely to monitor already. However, this outcome is only partially impacted by selective antibiotic susceptibility reporting, which impacts definitive antibiotic use or antibiotic use post-culture results. Therefore, our findings do not eliminate the possibility of this intervention influencing definitive antibiotic use. Rather, this study suggests that the changes in antibiotic use from this intervention in specific scenarios suggested by previous studies may not be detectable at the level of system-wide antibiotic use.

Whilst no significant change was detected among specific classes, trends indicating a potential decrease in carbapenem use and an increase in fluoroquinolone use warrant careful consideration. Carbapenem use has been linked to the development of carbapenem-resistant organisms [14] and therefore interventions to decrease their use can be highly valuable for ASPs. Increasing fluoroquinolone use, on the other hand, is a concerning signal given the plethora of adverse consequences secondary to their use, including *Clostridioides difficile* infection [15], antibiotic resistance [16] and adverse drug events [17–20]. Ultimately, changes in antibiotic use following the implementation of selective antibiotic susceptibility reporting are bound to be a reflection of the specific reporting rules and the antibiotics censored. The rules implemented at these hospitals were primarily targeted at suppressing broad-spectrum $\beta$-lactams for susceptible Gram-negative bacteria and non-glycopeptide anti-MRSA agents for susceptible Gram-

**Table 1**
Changes in antibiotic use by class.

| Class | Pre-intervention slope (DOT/1000-PD/month) (95% CI) | Post-intervention slope (DOT/1000-PD/month) (95% CI) | Step change (DOT/1000-PD) (95% CI) | Slope change (DOT/1000-PD/month) (95% CI) |
|---|---|---|---|---|
| Broad MDR | −0.19 (−2.46, 2.08) | 0.36 (−1.91, 2.62) | +8.75 (−19.03, 36.52) | +0.54 (−1.78, 2.87) |
| Non-glycopeptide anti-MRSA | −0.17 (−1.12, 0.78) | −0.05 (−0.95, 0.85) | +1.38 (−12.74, 15.50) | +0.12 (−0.80, 1.04) |
| Carbapenems | −0.11 (−0.90, 0.68) | −0.88 (−1.67, −0.08) | −4.65 (−14.30, 4.99) | −0.77 (−1.58, 0.05) |
| Non-carbapenem antipseudomonal $\beta$-lactams | 0.23 (−1.36, 1.82) | 1.26 (−0.32, 2.85) | +11.78 (−7.69, 31.24) | +1.03 (−0.59, 2.66) |
| 3G cephalosporins | −0.11 (−1.29, 1.08) | 0.17 (−0.99, 1.34) | +3.08 (−12.12, 18.24) | +0.28 (−0.92, 1.48) |
| 1/2G cephalosporins | 0.55 (−0.22, 1.32) | 0.01 (−0.81, 0.83) | −2.82 (−12.19, 6.56) | −0.55 (−1.39, 0.30) |
| Fluoroquinolones | −1.14 (−1.88, −0.39) | −0.45 (−1.20, 0.29) | +6.06 (−3.21, 15.33) | +0.68 (−0.08, 1.45) |
| Narrow–spectrum penicillins | −0.35 (−0.87, 0.16) | −0.26 (−0.77, 0.26) | +1.32 (−4.95, 7.59) | +0.10 (−0.43, 0.62) |

DOT, days of therapy; 1000-PD, 100 patient-days; CI, confidence interval; broad MDR, broad-spectrum agents for hospital-onset and multidrug-resistant infections; MRSA, methicillin-resistant *Staphylococcus aureus*; 3G, third-generation; 1/2G, first/second-generation.

positive bacteria. The study institutions should consider these data to guide possible revisions to the susceptibility reporting rules.

Additional limitations to this study include that only i.v. antibiotic use was measured and antibiotic stewardship interventions at the individual sites were not controlled for and therefore could have impacted the results. Due to variation in the timing of the intervention at each site, seasonality was not addressed.

Despite these limitations, this study adds to limited experience examining the large-scale effects of selective antibiotic susceptibility reporting on overall antibiotic use across a multihospital system. The inclusion of multiple hospitals increases the applicability of the results across different facility sizes and types. The interrupted time series analysis was appropriate for correcting for potential baseline underlying trends in antibiotic use prior to the intervention.

In conclusion, the implementation of selective antibiotic susceptibility reporting across seven hospitals had no impact on overall broad-spectrum i.v. antibiotic use. Further studies to determine the value of co-ordinated education with this intervention as well as its long-term impact are needed.

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## Competing interests

None declared.

## Ethical approval

Not required.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijantimicag.2019.06.011.

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