

## The Value of Hospital-Based Antimicrobial Stewardship Programs

### Background

Antimicrobial stewardship programs (ASPs) have been tasked with improving antimicrobial use to enhance patient outcomes, reduce antimicrobial cost, and minimize antimicrobial side effects. Several systematic reviews and meta-analyses have previously evaluated the impact of stewardship initiatives (i.e., restrictive versus persuasive interventions).<sup>1-3</sup> While these studies provide some insight on the magnitude of ASP effect, more data are needed to help individual ASPs determine how to demonstrate the potential impact of their work.

The purpose of this newsletter is to review a recent systematic review and meta-analysis of the impact of ASPs on antimicrobial use expressed in daily defined doses (DDD) per 1,000 patient days and subsequent clinical and economic outcomes.<sup>4</sup>

### Methods

This was a systematic review and meta-analysis including studies that reported data on the comparable efficacy of an ASP expressed in DDD/1,000 patient days before and after the intervention among hospitalized patients. All studies were independently evaluated by three separate reviewers. Discrepancies were discussed and resolved by consensus. The quality of study methods was assessed by two separate reviewers using a verified measurement tool. To ensure valid results, publication bias was assessed by Egger's test, a proven statistical method.

### Primary and Secondary Outcomes

The primary outcome was antimicrobial consumption before and after the implementation of an ASP in hospitals. Secondary outcomes included a series of clinical outcomes, including 30-day mortality rates, hospital and intensive care unit (ICU) lengths-of-stay (LOS), and changes in rate of *Clostridium difficile*

infections (CDI) and prevalence of antibiotic-resistant infections in the hospital. Additionally, the study assessed consistency of antimicrobial treatment with ASP or national guidelines and changes in cost of antimicrobial treatment.

### Results

A total of 149 studies were identified as potentially eligible, of which 26 studies (from 18 countries) were included in the meta-analysis. Most of the studies included were retrospective and/or prospective cohort studies. ASP strategies varied among studies and included preapproval strategies, prospective audit and feedback, education, guidelines, and formulary restrictions. Most ASPs employed multiple strategies simultaneously. Pre- and post-intervention periods lasted from 6 months to 3 years.

### Antimicrobial Consumption

Significant decreases in antimicrobial consumption were noted overall, as well as for restricted antimicrobials and many individual drug classes (**Table 1**). The overall change in antimicrobial consumption after ASP implementation was -19.1%, and this reduction was highest among studies conducted in the U.S. and Europe. A significant reduction in consumption of restricted antimicrobials, carbapenems, and glycopeptides (i.e., vancomycin) was observed after ASP implementation. Interestingly, this effect was not limited to antibacterial agents; antifungal consumption also decreased after ASP implementation despite the fact that only one out of six studies included had restrictions in place for antifungals. In regards to hospital setting, antimicrobial consumption was reduced by 12.1% in medical wards and 39.5% in the

**ASPs Reduced Antimicrobial  
Consumption by One-fifth!**

ICU. Consistency with ASP or national guidelines increased after ASP implementation (pooled risk difference [RD] = 0.078, 0.061 to 0.095).

**Table 1.** Changes in antimicrobial consumption following ASP implementation

Description	% change in consumption	No. studies reporting data
All antimicrobials	-19.1%	26
Restricted antimicrobials*	-26.6%	9
Carbapenems	-18.5%	11
Glycopeptides (vancomycin)	-14.7%	10
Antifungals	-39.1%	6

\*third- or fourth-generation cephalosporins, vancomycin, tigecycline, linezolid, imipenem, meropenem, and fluoroquinolones

## Infection Rates and Clinical Outcomes

The effect of implementing an ASP on the prevalence of resistant strains causing infections was evaluated. Overall, the prevalence of MRSA, imipenem-resistant *P. aeruginosa*, and ESBL-producing *Klebsiella spp.* was significantly lower following ASP implementation (**Table 2**). There was no difference observed in the prevalence of ESBL-producing *E. coli* infections. Similarly, there was no difference in the rate of CDI following ASP implementation. It is important to note this conclusion was drawn from only three studies reporting data, which should caution our interpretation of this finding. In a larger meta-analysis published in 2014 including 16 studies, a significant protective effect (pooled risk ratio 0.48, 95% CI: 0.38 to 0.62) was observed between ASPs and CDI.<sup>5</sup>

In regards to clinical outcomes, the mean hospital LOS was reduced by 8.9% (95% CI, -12.8 to -5) following ASP implementation; however, ICU LOS was not significantly changed. There was no change in overall nor infection-related 30-day mortality after ASP implementation.

**Table 2.** Resistant infection rates significantly impacted following ASP implementation.

Description	Change in prevalence (risk difference)	No. studies reporting data
MRSA	-0.017	6
Imipenem-resistant <i>P. aeruginosa</i>	-0.079	6
ESBL-producing <i>Klebsiella spp.</i>	-0.104	5

RD, risk difference; MRSA, methicillin-resistant *Staphylococcus aureus*; ESBL, extended-spectrum beta-lactamase

## Healthcare Resources

In addition to having significant impacts on antimicrobial consumption, infection rates, and clinical outcomes, implementation of ASPs also led to a significant reduction in antimicrobial cost. Specifically, the change in antimicrobial cost observed was -33.9% based on six studies reporting data (95% CI, -42% to -25.9%).

## DASON Discussion

Evaluating the impact of ASPs on meaningful outcomes remains challenging. This study provides stewards further information about how much impact an ASP can have on a variety of outcomes. The investigators showed significant decreases in antimicrobial consumption after ASP implementation, which is widely accepted as a method to address increasing resistance and adverse events, such as CDI. In addition, antimicrobial cost was reduced and patient outcomes were improved. Another strength of this study is its inclusion of a wide variety of practice settings. Studies included hospitals from 18 countries, ranging from 200-bed community hospitals to 2,000-bed academic medical centers. This study provides useful information to help choose which outcomes to track for evaluating the impact of local efforts and demonstrate the value of an ASP for hospital leadership. Knowing ASPs can impact these important outcomes should give us the confidence to demonstrate these improvements in our own hospitals.

While the results of this meta-analysis are encouraging, there are several limitations worth discussing. First, most

systematic reviews and meta-analyses suffer from limitations caused by the substantial heterogeneity among included studies. In other words, the types of stewardship initiatives vary considerably in their design and implementation. In the end, it becomes difficult to discern which stewardship initiatives, in particular, impact the outcome of interest. This study has the same limitation. Second, while antimicrobial consumption was decreased, the appropriateness of antimicrobial use was not evaluated. Thus, we cannot conclude the impact of ASPs on antimicrobial consumption resulted in more appropriate use. Lastly, without randomized controlled trials, no direct inference can be drawn on the causal relationship between stewardship initiatives and outcomes. Despite these limitations, the size of ASP impact is substantial and this information is useful.

## Conclusion

Overall, this review provides evidence that the collective efforts of ASPs, despite being variable in clinical practice, have a significant impact on antimicrobial consumption as well as clinical and economic outcomes. Current research efforts at DASON are focused on defining metrics to demonstrate ASP impact and then use them to help drive decisions on program implementation. We are excited for the opportunity to continue collaborating with our community hospital partners to optimize antimicrobial prescribing in our patients and further develop metrics to describe the impact of our work.

## Take Home Points:

1. Implementing in-hospital ASPs resulted in an overall reduction in antimicrobial use by 19.1%, and this effect was nearly doubled (39.1%) in ICU settings
2. Use of restricted antimicrobials, such as carbapenems and vancomycin were significantly reduced
3. Antimicrobial cost and hospital length-of-stay were significantly reduced
4. Infections caused by MRSA, imipenem-resistant *Pseudomonas aeruginosa*, and ESBL-producing *Klebsiella spp.* were significantly less

## References

1. Davey P, Brown E, Charani E, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev.* 2013(4):CD003543.
2. Wagner B, Filice GA, Drekonja D, et al. Antimicrobial stewardship programs in inpatient hospital settings: a systematic review. *Infect Control Hosp Epidemiol.* 2014;35(10):1209-1228.
3. Schuts EC, Hulscher ME, Mouton JW, et al. Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis. *Lancet Infect Dis.* 2016;16(7):847-856.
4. Karanika S, Paudel S, Grigoras C, Kalbasi A, Mylonakis E. Systematic Review and Meta-analysis of Clinical and Economic Outcomes from the Implementation of Hospital-Based Antimicrobial Stewardship Programs. *Antimicrob Agents Chemother.* 2016;60(8):4840-4852.
5. Feazel LM, Malhotra A, Perencevich EN, Kaboli P, Diekema DJ, Schweizer ML. Effect of antibiotic stewardship programmes on *Clostridium difficile* incidence: a systematic review and meta-analysis. *J Antimicrob Chemother.* 2014;69(7):1748-1754.

## dason news

- MARK YOUR CALENDARS! The DASON/DICON Fall 2016 Symposium will be held on Friday, November 18 at the Sheraton Greensboro Hotel at Four Seasons from 8:30AM-3:30PM – We look forward to seeing you there!