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Original Article

Assessing the impact of antibiotic stewardship program elements on antibiotic use across acute-care hospitals: an observational study

Bradley J. Langford BScPhm, ACPR, PharmD, BCPS[1,2], Julie Hui-Chih Wu MSc[1], Kevin A. Brown PhD[1,3], Xuesong Wang MSc[4], Valerie Leung BScPhm, ACPR, MBA[1], Charlie Tan MD[5], Gary Garber MD, FRCPC, FACP, FIDSA, CCPE[1,3,6,7] and Nick Daneman MD, FRCPC, MSc[1,3,4,8,9]

[1]Public Health Ontario, Toronto, Canada, [2]St Joseph's Health Center, Toronto, Canada, [3]University of Toronto, Toronto, Canada, [4]Institute for Clinical Evaluative Sciences, Toronto, Canada, [5]London Health Sciences Center, London, Canada, [6]University of Ottawa, Ottawa, Canada, [7]Ottawa Hospital Research Institute, Ottawa, Canada, [8]Division of Infectious Diseases, Sunnybrook Health Sciences Center, Toronto, Canada and [9]Sunnybrook Research Institute, Sunnybrook Health Sciences Center, Toronto, Canada

Abstract

Objectives: Antibiotic use varies widely between hospitals, but the influence of antimicrobial stewardship programs (ASPs) on this variability is not known. We aimed to determine the key structural and strategic aspects of ASPs associated with differences in risk-adjusted antibiotic utilization across facilities.
Design: Observational study of acute-care hospitals in Ontario, Canada
Methods: A survey was sent to hospitals asking about both structural (8 elements) and strategic (32 elements) components of their ASP. Antibiotic use from hospital purchasing data was acquired for January 1 to December 31, 2014. Crude and adjusted defined daily doses per 1,000 patient days, accounting for hospital and aggregate patient characteristics, were calculated across facilities. Rate ratios (RR) of defined daily doses per 1,000 patient days were compared for hospitals with and without each antimicrobial stewardship element of interest.
Results: Of 127 eligible hospitals, 73 (57%) participated in the study. There was a 7-fold range in antibiotic use across these facilities (min, 253 defined daily doses per 1,000 patient days; max, 1,872 defined daily doses per 1,000 patient days). The presence of designated funding or resources for the ASP ($RR_{adjusted}$, 0.87; 95% CI, 0.75–0.99), prospective audit and feedback ($RR_{adjusted}$, 0.80; 95% CI, 0.67–0.96), and intravenous-to-oral conversion policies ($RR_{adjusted}$, 0.79; 95% CI, 0.64–0.99) were associated with lower risk-adjusted antibiotic use.
Conclusions: Wide variability in antibiotic use across hospitals may be partially explained by both structural and strategic ASP elements. The presence of funding and resources, prospective audit and feedback, and intravenous-to-oral conversion should be considered priority elements of a robust ASP.

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Antimicrobial resistance is a significant threat to public health. It results in decreased effectiveness of antimicrobial therapy leading to prolonged illness, increased mortality, and increased social and economic costs.[1] Antimicrobial utilization, the key driver of resistance, is highest in acute-care settings. However, up to 50% of this use is considered inappropriate.[2] Implementing an antimicrobial stewardship program (ASP) is a vital intervention to address inappropriate use and prevent the negative consequences of therapy in this setting.[3]

Guidelines have promoted the importance of both structural (eg, funding, staffing, leadership support) and strategic (eg, interventions to improve antimicrobial utilization) ASP components.[3,4] Despite recommendations to include these components in a hospital ASP, their relative impact remains to be determined. Additionally, identifying which elements may influence antibiotic use is an important consideration in the context of finite hospital resources where prioritizing ASP activities is needed.

Recent studies indicate that antimicrobial utilization varies widely between hospital facilities even after accounting for nonmodifiable factors (eg, hospital type, patient population characteristics).[5,6] Current knowledge about the drivers of such variability is limited, particularly as it relates to the impact of an ASP on antimicrobial use.

The primary objective of this study was to determine whether the following hospital ASP structural elements are associated with reduced antibiotic use: program maturity, designated funding/resources, recognition as an organizational priority, and reporting of ASP metrics to senior administration. A secondary objective was to determine which specific strategies strongly recommended by the 2016 Infectious Diseases Society of America (IDSA)/Society for Healthcare Epidemiology of America (SHEA) guidelines are associated with reduced antibiotic use: formulary restriction with

Author for correspondence: Bradley J. Langford, Public Health Ontario, 480 University Ave, Toronto, ON, Canada, M5G 1V2. E-mail: Bradley.langford@oahpp.ca

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preauthorization, prospective audit and feedback, therapeutic drug monitoring with feedback, and intravenous-to-oral conversion.[3]

Methods

Study design and setting

We conducted an observational study of acute-care hospitals in Ontario, Canada, to evaluate the association between self-reported ASP characteristics in place as of 2013 and risk-adjusted antibiotic utilization for the 2014 calendar year.

Antimicrobial stewardship program survey

The Ontario ASP Landscape survey, developed by Public Health Ontario, asked clinicians about the structural and strategic elements of their organization's ASP (Table 1). The survey was pilot tested by selected individuals involved in hospital ASPs (eg, pharmacists, program leads) and was refined based on their feedback prior to dissemination. The voluntary survey, administered online and open for 5 weeks (September–October, 2016), was distributed to all hospitals and was addressed to the individual most responsible for antimicrobial stewardship in their organization (eg, ASP pharmacist or physician). Respondents were asked the year of ASP element implementation. Only elements implemented in 2013 or prior were considered present for the purposes of this analysis. The ASP elements implemented in 2014 and later or with year unknown were considered absent (due to respondent uncertainty of whether these elements were present prior to 2014).

Table 1. Structural and Strategic Antimicrobial Stewardship Program (ASP) Elements

Structural Elements of ASP (n = 8)
• Presence vs. absence of formal ASP
• Maturity of ASP (in place for at least 3 years)
• Designated funding/resources for ASP
• Presence of a physician champion
• Presence of a pharmacist champion
• Presence of an antimicrobial stewardship committee (ASC)
• Metrics reported to senior administration
• Recognition as an organizational priority (antimicrobial use is part of the organization's quality improvement plan and/or a strategic goal/priority)
Strategic Elements of ASP (n = 32)
Formulary-related Strategies
• Formulary automatic substitution/therapeutic interchange policies
• Formulary restriction
• Formulary restriction with preauthorization
• Formulary review/streamlining
Process Strategies
• Automatic stop orders
• Checklists
• Drug use evaluation/medication use evaluation
• General antimicrobial order forms
• Improved antimicrobial documentation
• Surgical antibiotic prophylaxis optimization
• Systematic antibiotic allergy verification
Clinical Strategies
• De-escalation and streamlining
• Dose optimization
• Identification of inappropriate pathogen/antimicrobial combinations
• Preventing treatment of noninfectious conditions
• Prospective audit and feedback
• Scheduled antimicrobial reassessments
• Targeted review of patients with *Clostridium difficile* infection
• Targeted review of patients with bacteremia/fungemia
• Targeted review of redundant therapy or therapeutic duplication
• Therapeutic drug monitoring (with feedback)
Prescribing Guidance Strategies
• Clinical decision support systems/computerized physician order entry
• Disease-specific treatment guidelines/pathways/algorithms and/or order forms
• Empiric antibiotic prescribing guidelines
• Facilitation of appropriate and timely antimicrobial administration in severe sepsis/septic shock
• intravenous-to-oral conversion
• Prescriber education
Microbiology-Related Strategies
• Antibiograms
• Cascading microbiology susceptibility reporting
• Improved diagnostics
• Promotion of timely and appropriate microbiologic sampling
• Strategic microbiology results reporting

Antibiotic use

Monthly antibiotic purchasing from January 1 to December 31, 2014, for acute-care hospitals in Ontario was included in this dataset in grams for each antibiotic and was converted to defined daily doses, a standard metric defined by the World Health Organization for benchmarking drug utilization.[7] All systemic antibacterials administered by the enteral or parenteral route were included. Purchasing data were obtained from the IMS Health Canadian Drug Store and Hospital Purchases Audit, which includes direct and indirect drug sales to hospitals and pharmacies across Canada. These data have been validated, showing a strong correlation with internal hospital records of antibiotic dispensing (correlation coefficient, 0.88–0.91).[8]

Data on acute-care hospitals and hospitalizations

Eligible hospitals included acute-care facilities in Ontario. Hospitals that specialized only in psychiatric, surgical, pediatric, outpatient, rehabilitation or long-term geriatric care were excluded given the anticipated low rates of antibiotic use and the paucity of antibiotic stewardship efforts. Two hospitals that purchased antibiotics for nursing station outposts in their area were excluded because their inpatient antibiotic use would be overestimated. Hospitals with shared purchasing or pooled administrative data were combined (eg, multiple hospital sites within a hospital corporation). Hospital-level variables collected for this study were based on a previous work of risk-adjusted variability in hospital antibiotic use in Ontario.[5] The number of patient days from inpatient admissions and same-day surgeries in 2014 at each hospital were obtained from Canadian Institutes of Health Information Discharge Abstracts Database and Same-Day Surgery databases, respectively. Hospital characteristics collected are shown in Table 2.

Privacy and ethics

The Privacy Office and Ethics Review Board at Public Health Ontario approved this study.

Primary outcome

Antibiotic use was expressed in defined daily doses per 1,000 patient days at each hospital.

Statistical analysis

A multivariable generalized estimating equations (GEE) Poisson regression model, using defined daily doses as the outcome and the log of hospital patient days as the offset, was developed. The model included the hospital and patient covariates from the administrative databases (Table 2) using an exchangeable correlation structure. The best-fitting model was generated by backward selection, with prespecified, forced inclusion of hospital type, proportion of admissions by service, proportion of admissions that included an ICU stay, and proportion of admissions by patient age.[5] The observed (O) antibiotic use at each hospital was compared to the model-based expected (E) antibiotic use, and hospitals were ranked from lowest to highest according to the O:E ratio. Analyses were performed with SAS Enterprise Guide version 7.12 software (SAS Institute, Cary, NC).

Table 2. Hospital Characteristics

- Hospital type
- Location
- Resource intensity weight
- Presence of infectious diseases physician
- Length of hospital stay
- Proportions of admissions by service, and
- Proportion of admissions that were elective, transferred from acute-care hospitals and that included an ICU stay
- Aggregate patient characteristics (age, sex)

Note. ICU, intensive care unit.

Results

Hospital characteristics and antibiotic use

Of 127 eligible hospitals, 73 (57%) participated in this study. Among these 73 facilities were 12 academic teaching hospitals (16%), 36 large community hospitals (49%), 17 medium community hospitals, (23%) and 8 small community hospitals (11%). Wide variability (7-fold) in antibiotic usage was observed, ranging from 253 to 1,872 defined daily doses per 1,000 patient days. Table 3 displays hospital and aggregate patient characteristics of the hospitals, subdivided into quintiles of O:E ratio of antibiotic use.

Table 3. Hospital Characteristics Ranked by Observed to Expected Antibiotic Use Ratio (Lowest to Highest)

Characteristic	Overall	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
No. of facilities	73	14	15	15	15	14
Median O:E ratio	1.0	0.7	0.9	1.0	1.2	1.5
Median DDD/1,000 PD	491.5	366.3	436.0	479.9	578.9	758.4
Hospital type, no. (%)						
Academic teaching or large community	48 (65.8)	11 (78.6)	9 (60.0)	12 (80.0)	10 (66.7)	6 (42.9)
Admitting service, % (IQR)						
Medical	23.4 (19.6–31.5)	21.9 (19.6–26.9)	24.5 (20.3–31.5)	25.9 (19.0–31.2)	22.6 (19.5–36.9)	34.2 (17.6–41.8)
Surgical	60.8 (52.3–68.3)	64.8 (58.8–71.0)	60.8 (49.6–64.2)	59.5 (53.0–68.3)	58.0 (43.0–66.5)	55.2 (24.8–69.3)
Maternal/Obstetric	6.3 (2.4–8.1)	4.6 (2.5–7.7)	6.4 (3.1–8.1)	7.1 (0.0–8.3)	7.3 (4.7–10.0)	3.0 (0.2–6.7)
Neonatal	6.2 (1.8–7.5)	4.6 (2.2–7.1)	6.3 (2.5–7.7)	6.9 (0.0–8.1)	7.0 (4.5–9.7)	2.3 (0.2–6.6)
Mental health	1.2 (0.7–1.8)	1.2 (0.7–1.3)	1.1 (0.9–2.7)	1.1 (0.6–1.5)	1.3 (0.6–2.7)	1.1 (0.4–4.4)
Elective admissions, % (IQR)	64.6 (55.9–68.1)	66.9 (61.0–69.3)	64.4 (54.1–67.3)	60.7 (55.9–70.3)	64.6 (55.9–67.8)	60.3 (34.9–69.7)
Admissions with ICU stay, % (IQR)	4.3 (2.5–6.7)	4.5 (3.4–5.8)	4.3 (0.0–6.9)	6.1 (3.6–9.6)	4.1 (0.7–6.7)	3.0 (0.0–5.0)
Transfers from other acute-care hospitals, % (IQR)	1.9 (1.2–3.3)	1.7 (1.4–2.8)	1.9 (1.2–2.6)	2.7 (0.9–3.8)	2.4 (0.9–3.5)	2.7 (1.4–3.8)
Patient age, mean y (SD)	54.53 ± 6.80	55.31 ± 3.93	53.40 ± 5.62	55.31 ± 6.81	51.56 ± 8.94	57.32 ± 7.00
Patient age, % (IQR)						
<18 y	9.5 (4.7–13.0)	8.5 (4.1–12.4)	10.9 (6.4–13.5)	10.1 (1.8–14.4)	10.3 (7.5–15.3)	4.6 (1.3–11.8)
18–65 y	51.8 (49.2–54.8)	53.0 (51.7–55.9)	52.3 (47.7–54.7)	51.2 (49.2–54.8)	50.9 (43.7–55.9)	50.7 (43.5–53.0)
>65 y	38.0 (33.5–44.2)	37.6 (35.1–41.6)	38.1 (31.8–42.0)	36.8 (33.6–48.4)	39.3 (28.0–42.6)	37.3 (33.9–52.6)
Female patients, mean (SD)	54.9 (52.4–56.6)	53.1 (52.2–54.5)	56.4 (53.9–57.4)	54.3 (49.6–56.9)	56.5 (55.5–57.8)	54.2 (48.3–55.6)
Length of stay, % (SD)						
≤2 d	72.9 (68.5–78.6)	73.5 (70.6–78.3)	75.4 (70.1–78.8)	75.5 (64.7–78.3)	74.2 (69.0–78.6)	71.7 (66.4–79.7)
≥10 d	7.4 (5.5–8.5)	7.3 (5.6–8.2)	6.3 (5.2–8.1)	8.0 (5.3–11.5)	7.1 (5.4–8.2)	7.8 (5.6–9.7)
Resource intensity weight, mean (SD)	0.83 ± 0.39	0.81 ± 0.21	0.79 ± 0.41	0.88 ± 0.34	0.81 ± 0.42	0.83 ± 0.53

Note. O:E observed to expected; DDD, defined daily dose; PD, patient days; IQR, interquartile ratio; SD, standard deviation.

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Antimicrobial stewardship program characteristics

Structural elements

Of the 73 hospitals participating, 24 hospitals (33%) implemented 0–2 structural elements, 22 hospitals (30%) implemented 3–5 structural elements, and 27 hospitals (37%) implemented 6–8 structural elements. 49 hospitals (67%) reported implementation of a formal ASP. Among these programs, 23 hospitals (47%) were mature ASPs (ie, in place for at least 3 years). With respect to other structural characteristics, 33 hospitals (45%) had dedicated ASP funding and/or resources; 19 hospitals (26%) had ASP recognized as an organizational priority; 31 hospitals (42%) reported ASP metrics to senior administration.

Strategic elements

Of the 32 ASP strategies, 15 hospitals (21%) implemented 0–7 ASP strategies, 22 hospitals (30%) implemented 8–15 ASP strategies, and 36 hospitals (49%) implemented 16 or more ASP strategies. Regarding strategies strongly recommended by IDSA/SHEA, formulary restriction with preauthorization was implemented by 15 hospitals (21%), prospective audit and feedback was implemented by 42 hospitals (58%), therapeutic drug monitoring with feedback was implemented by 53 hospitals (73%), and intravenous-to-oral conversion was implemented by 47 hospitals (64%).

Impact of ASP elements on outcome

Structural elements

After adjustment for hospital and patient characteristics, the only structural element associated with lower risk-adjusted antibiotic use was the presence of designated ASP funding or resources (Fig. 1). This element was associated with modestly lower antibiotic use (rate ratio [RR], 0.87; 95% CI, 0.75–0.99). The overall number of structural characteristics implemented was not statistically significantly associated with lower antibiotic use.

Strategic elements

The IDSA/SHEA-recommended strategies of prospective audit and feedback (RR, 0.80; 95% CI, 0.67–0.96) and intravenous-to-oral conversion (RR, 0.79; 95% CI, 0.64–0.99) were associated with lower risk-adjusted antibiotic use (Fig. 2). Hospitals with 16 or more strategies were associated with lower antibiotic use (RR, 0.76; 95% CI, 0.64–0.90), but statistical significance was lost (RR, 0.82; 95% CI, 0.65–1.04) after adjustment for hospital and patient characteristics.

Discussion

This analysis of 73 Ontario hospitals revealed that key structural and strategic ASP elements are significantly associated with decreased hospital antibiotic utilization. These elements were the presence of designated funding or resources, prospective audit and feedback, and intravenous-to-oral conversion.

These results echo previous findings that ASP characteristics contribute to variability in antibiotic use between hospitals. Pakyz *et al.*[9] found that an antimicrobial stewardship strategy score was associated with lower antibiotic use across 44 academic medical centers in the United States.[9] Although our study did not find an

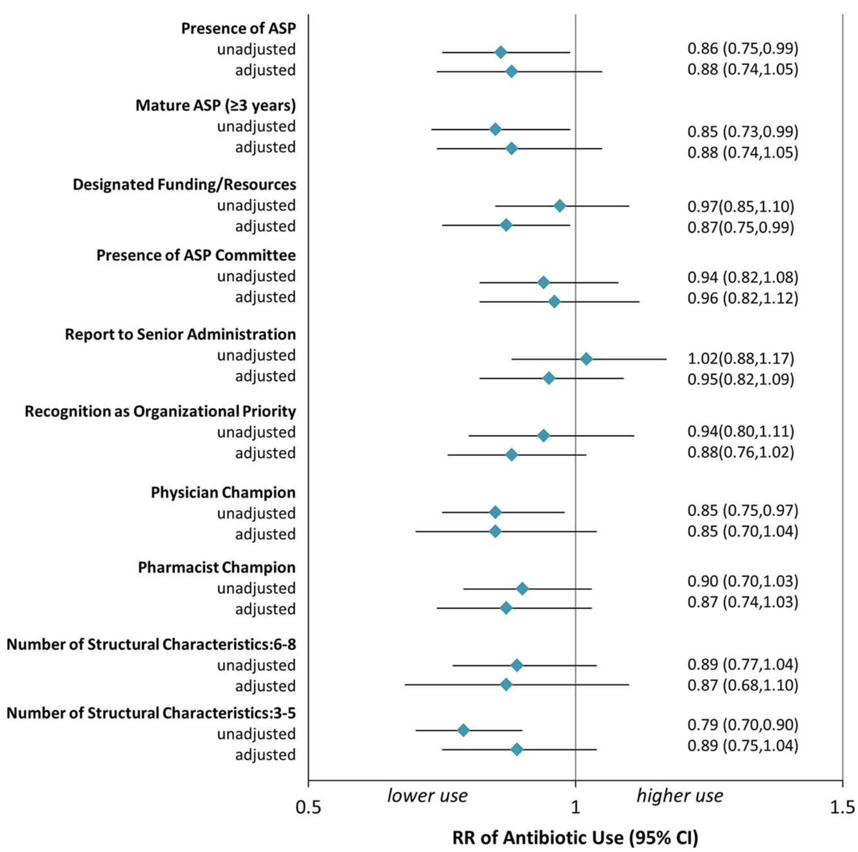

Fig. 1. Impact of antibiotic stewardship program (ASP) structural elements on antibiotic use. Forest plot of the rate ratio (RR) of unadjusted and adjusted antibiotic use measured in defined daily doses (DDD) per 1,000 patient days (PD) for hospitals with specified ASP characteristics. The reference is the absence of the characteristic, and for the number of structural characteristics it is 0–2 elements.

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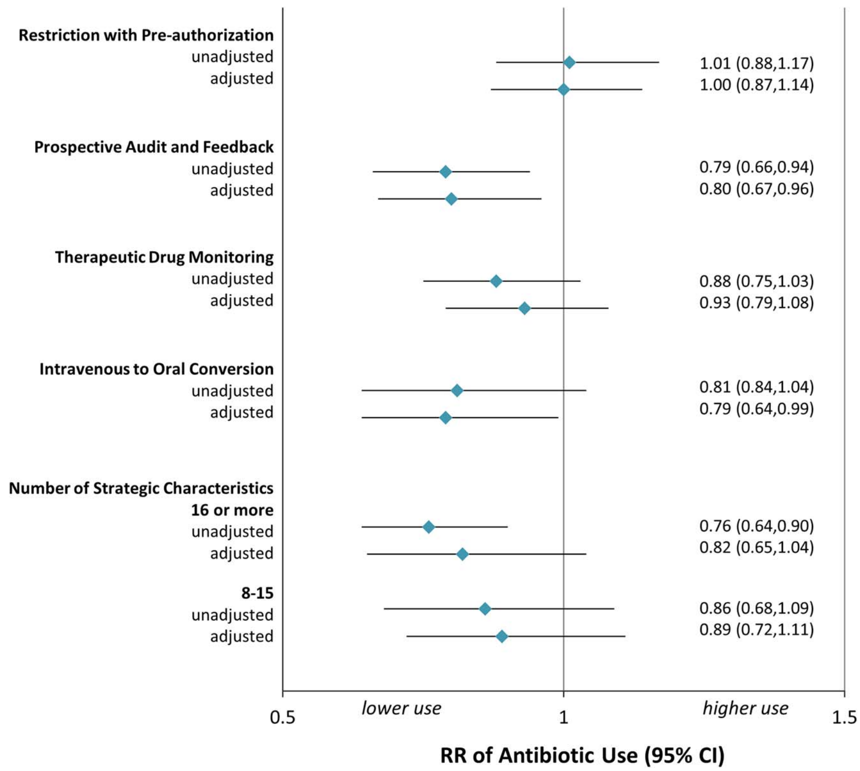

Fig. 2. Impact of antibiotic stewardship program (ASP) strategic elements on antibiotic use. Forest plot of the rate ratio (RR) of unadjusted and adjusted antibiotic use measured in defined daily doses (DDD) per 1000 patient days (PD) for hospitals with specified ASP characteristics. The reference is the absence of the characteristic, and for the number of strategic characteristics it is 0–7 elements.

association between the overall number of strategies and antimicrobial use, both studies found that prospective audit and feedback was a predictor of reduced antibiotic use. In contrast, a study of 977 acute-care hospitals in France found no association between their "action score," a measure of strategies implemented, and antibiotic usage. However, they found an association between the hospital's "resource score," an indicator of personnel and technological support, and antibiotic consumption.[10] Predictors of antibiotic use variability differ across studies, which may reflect differences in definitions of ASP components, scoring systems used, risk-adjustment, and geography. Nevertheless, the literature to date supports the recommendations by the IDSA/SHEA and CDC that both structural and strategic characteristics must be considered when building an ASP.

Presence of ASP funding and/or resources was associated with modestly lower antibiotic use. The independent impact of this structural element is difficult to assess given that ASP resources allow for more robust implementation of strategies, the latter of which are expected to drive changes in antibiotic prescribing. However, evidence shows that ASPs without funding and/or resources may be less able to impact antibiotic prescribing through strategies such as prospective audit and feedback.[11] Although we detected a trend toward reduced antibiotic use in programs with pharmacist and physician champions, these elements were not associated with reduced antibiotic use in the adjusted analysis. Pharmacist and physician leadership of ASPs is certainly important, but they are most likely to be effective when having protected time to perform ASP duties, further underscoring the need for dedicated ASP personnel.

A recent Cochrane review examining interventions to improve antibiotic prescribing in hospital settings found that both restrictive and enabling (advice or feedback to guide prescribing) were effective at improving antibiotic use and reducing length of stay without increasing mortality.[12] Furthermore, enabling approaches tended to amplify the impact of other interventions, including antimicrobial restrictions. We did not find an association between restrictions and antibiotic use, but we did find that the enabling intervention of prospective audit and feedback was a predictor of lower antibiotic use.

Importantly, 2 interventions strongly recommended by the IDSA/SHEA were associated with low antibiotic utilization: prospective audit and feedback and intravenous-to-oral conversion. Although prospective audit and feedback has a proven impact on antimicrobial utilization,[13,14] the mechanism by which intravenous-to-oral conversion can reduce antibiotic consumption is less certain. One reason for this finding could be reduced length of stay[15] for patients receiving antimicrobial agents, allowing for earlier discharge and shifting use to the outpatient setting. Alternatively, intravenous-to-oral strategies may be indirect markers of more robust ASPs.

Our study does have some limitations. There may be selection bias given that only 57% of eligible hospitals participated. Our model risk-adjusted antibiotic use at the facility level, but given the observational nature of the study, unmeasured confounding may have occurred. Factors that may influence antibiotic use patterns, such as percentage of cystic fibrosis, oncology, and organ transplantation patients, were not considered. On the other hand, in this study, antibiotic use tended to be higher in community hospitals where these populations are less likely to be found. Due to the self-reported nature of the survey, the fidelity and degree of implementation of each ASP element was not assessed, which although challenging to quantify, could be an important factor impacting antibiotic use. Validating the survey responses with measures of actual implementation would be ideal for future studies. Finally, our study did not assess the appropriateness of antibiotic therapy. This is a labor-intensive activity and presents challenges in cases where appropriateness is uncertain. However, given that an estimated 50% of antibiotic use is inappropriate, a downward trajectory in antibiotic use is likely reflective of reductions in inappropriate use.

Despite these limitations, this study offers important considerations for ASPs in hospital settings, including key structural and strategic elements that may reduce inappropriate antimicrobial exposure for patients.

In conclusion, wide variability in antibiotic use across hospitals may be partially explained by ASP characteristics. Both structural elements (ie, designated funding/resources) and strategic elements (ie, prospective audit and feedback, intravenous-to-oral conversion) are associated with reduced risk-adjusted antibiotic use.

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Conflicts of interest. All authors report no conflicts of interest relevant to this article.

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