ORIGINAL ARTICLE

Prevalence and Characteristics of Antimicrobial Stewardship Programs at Freestanding Children's Hospitals in the United States

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BACKGROUND AND OBJECTIVE. Antimicrobial stewardship programs (ASPs) are a mechanism to ensure the appropriate use of antimicrobials. The extent to which ASPs are formally implemented in freestanding children's hospitals is unknown. The objective of this study was to determine the prevalence and characteristics of ASPs in freestanding children's hospitals.

METHODS. We conducted an electronic survey of 42 freestanding children's hospitals that are members of the Children's Hospital Association to determine the presence and characteristics of their ASPs. For hospitals without an ASP, we determined whether stewardship strategies were in place and whether there were barriers to implementing a formal ASP.

RESULTS. We received responses from 38 (91%) of 42. Among responding institutions, 16 (38%) had a formal ASP, and 15 (36%) were in the process of implementing a program. Most ASPs (13 [81%] of 16) were started after 2007. The median number of full-time equivalents dedicated to ASPs was 0.63 (range, 0.1–1.8). The most common antimicrobials monitored by ASPs were linezolid, vancomycin, and carbapenems. Many hospitals without a formal ASP were performing stewardship activities, including elements of prospective audit and feedback (9 [41%] of 22), formulary restriction (9 [41%] of 22), and use of clinical guidelines (17 [77%] of 22). Antimicrobial outcomes were more likely to be monitored by hospitals with ASPs (100% vs 68%; $P = .01$), although only 1 program provided support for a data analyst.

CONCLUSIONS. Most freestanding children's hospitals have implemented or are developing an ASP. These programs differ in structure and function, and more data are needed to identify program characteristics that have the greatest impact.

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Antimicrobial stewardship programs (ASPs) are hospital-based interventions designed to optimize antimicrobial use. By requiring prior authorization for or structured post-prescription review of antimicrobial prescribing, ASPs reduce antimicrobial overuse and prescribing errors, which leads to improvements in the quality and safety of clinical care while lowering costs.[1] Reducing unnecessary antibiotic prescribing is especially important in light of increasing rates of drug-resistant infections with few new antimicrobials under development.[2] In 2007, the Infectious Diseases Society of America (IDSA) recommended that all hospitals develop ASPs and provided guidelines for ASP development; the guidelines were endorsed by the Pediatric Infectious Diseases Society and the American Academy of Pediatrics.[1]

A study conducted soon after publication of the IDSA guidelines for ASPs showed that implementation of pediatric ASPs was limited.[3] However, many free-standing children's hospitals without formal programs were in the early stages of ASP development and implementation.[3] Several single-center pediatric studies have demonstrated significant benefits following ASP implementation, including cost reductions, decreased nonapproved use of antibiotics, and decreased missed

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or delayed doses, although these programs used different structures.[4-6] The 2 general strategies employed by ASPs, which are not mutually exclusive, include (1) prior authorization, where selected antimicrobials require approval before they can be prescribed, and (2) prospective audit and feedback, where antimicrobial use is reviewed and feedback offered to the prescribing physician after a designated period of time (eg, 48–72 hours).

Freestanding children's hospitals account for more than 20% of pediatric hospitalizations in the United States. The extent to which ASPs have been implemented in these institutions since the publication of guidelines in 2007 remains unknown. The objective of this study was to describe ASP activities within a large, nationwide network of freestanding children's hospitals, including details about program structure, available resources, implementation barriers and outcomes monitored. This information will provide the framework for future investigations to determine the program structure and strategies that have the greatest impact on ASP outcomes as well as to strengthen the evidence base detailing the impact of ASP activities on antimicrobial use.

METHODS

Study Design Population

In June 2011, we conducted a survey of the 42 hospitals within the Children's Hospital Association (CHA) that contribute data to the Pediatric Health Information Systems (PHIS) database. These freestanding children's hospitals represent 17 of the 20 major metropolitan areas within the United States and account for 75% of all freestanding children's hospitals and 15%–20% of all pediatric hospitalizations in the United States.[7] In accordance with the Common Rule (45 CFR 46.102(f)) and the policies of the Children's Mercy Hospitals and Clinics, this study was not considered human subjects research.

The survey was distributed electronically to 1 representative from each of the 42 hospitals participating in CHA. For those institutions with ASPs, the survey was completed by the infectious diseases physician or pharmacist leading the program. For institutions developing a program, we identified the anticipated physician leader for the program. For institutions without an ASP, respondents were either the hospital epidemiologist or another individual determined to be most knowledgeable about antimicrobial prescribing practices. Up to 2 follow-up queries were sent at 1-week intervals to nonrespondents.

Survey Development

The survey was designed by infectious diseases physicians with direct experience in ASP development and management. Questions were developed, in part, on the basis of earlier surveys regarding ASPs and guidelines discussing the development of ASPs in hospital settings. To gather additional qualitative information, 2 focus groups were conducted in June 2011 at the second annual Pediatric Antimicrobial Stewardship Conference held in Kansas City, Missouri. The discussion generated by the focus groups served to expand and validate the existing survey template. The survey was pilot tested by a convenience sample of 10 infectious diseases physicians.

The survey first classified institutions by the presence or absence of an ASP. We defined an ASP as a comprehensive program that functions continuously to monitor antimicrobial use and that dedicates full-time equivalents (FTEs) to support a clinical pharmacist and/or pediatric infectious diseases specialist. For institutions without an ASP, we also as-

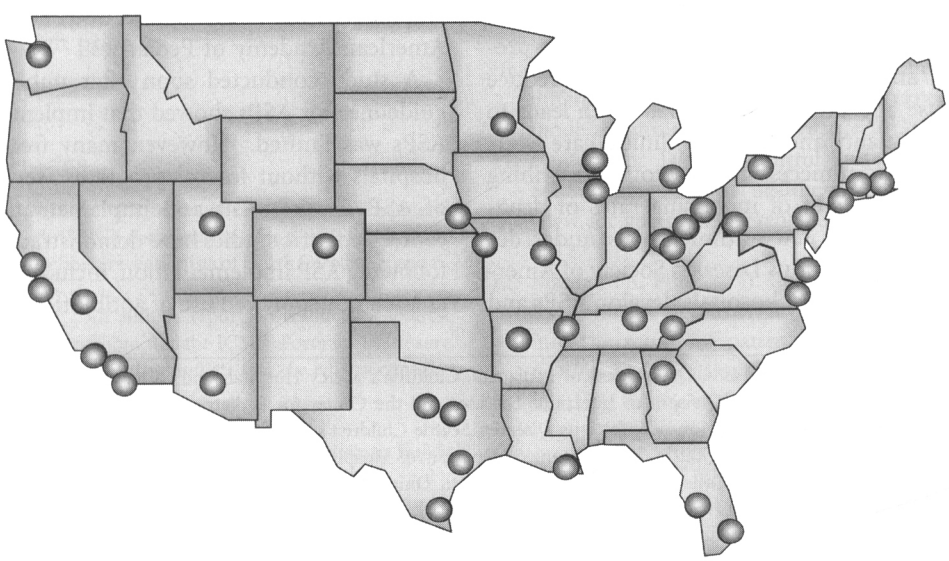

FIGURE 1. Geographic locations of freestanding children's hospitals that responded to the survey.

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TABLE 1. Demographic Data of Hospitals with and without an Antimicrobial Stewardship Program (ASP) as of 2007

Variable	Hospitals without ASP (n = 22)	Hospitals with ASP (n = 16)	P
Bed size	242 (203–265)	295 (256–338)	.017
Case mix index	2.6 (2.3–3.0)	2.8 (2.4–2.9)	.383
Total patient-days	69,894 (55,844–78,117)	90,280 (78,632–98,553)	.002
NICU days, %	20 (13.7–27.7)	16.1 (4.4–21.9)	.198
PICU days, %	11.5 (8.5–14.7)	11.6 (10.1–15.5)	.487
Surgical patient-days, %	23.8 (22.0–27.8)	25.9 (22.9–31.5)	.383
Solid organ transplantation	10 (0–39)	32 (16–51)	.005
Bone marrow transplantation	24 (1–35)	34 (18–67)	.169
Census region, no. (%) of hospitals			.776
Northeast	2 (9.1)	3 (18.8)	...
South	8 (36.4)	4 (25.0)	...
North central	6 (27.3)	5 (31.3)	...
West	6 (27.3)	4 (25.0)	...

NOTE. Data are median value (interquartile range), unless otherwise indicated. NICU, neonatal intensive care unit; PICU, pediatric intensive care unit.

certained whether a program was currently under development. For hospitals with an ASP, respondents indicated the year that the program was initiated and the number of FTEs dedicated for the infectious diseases physician, infectious diseases pharmacist(s), and data analyst. Respondents indicated whether one or both of the 2 core ASP strategies (prospective audit with feedback and/or prior approval/formulary restriction) were used and which antimicrobials were monitored. We also determined whether these strategies were employed at institutions that did not have an ASP. For institutions without an ASP, we inquired about the barriers to developing and implementing a program.

Additionally, for all institutions, we asked about the use of other ASP strategies considered valuable in managing the use of antimicrobials, including clinical guidelines, antibiotic order forms, and information technology solutions. Respondents indicated whether they had electronic health records (EHRs), computer physician order entry (CPOE), and clinical decision support software used for infection prevention and/or antimicrobial stewardship. Finally, we asked all hospitals about the outcomes that they monitored, including antimicrobial use, antimicrobial costs, antimicrobial resistance, compliance with ASP recommendations, and rate of *Clostridium difficile* infection.

Hospital Characteristics

Data were obtained from PHIS to determine the characteristics of the hospitals in 2007, which was the year that the IDSA ASP guideline was published. We selected this date because it reflected hospital activities at a time when attention to ASPs was beginning to increase. The hospital characteristics included total number of beds, total patient-days, percentage of patient-days spent in the neonatal intensive care unit (NICU) and pediatric intensive care unit (PICU), percentage of surgical patient-days, case mix index (a CHA-derived proxy for severity of illness), and number of bone marrow transplantations and solid-organ transplantations performed at these hospitals. Solid-organ transplantations included kidney, heart, liver, and small bowel transplantations.

Data Analysis

Descriptive statistics were used to describe characteristics of the hospitals in the survey. $\chi 2$ tests or Fisher exact tests, when indicated, were used to compare categorical characteristics between hospitals with and without an ASP. Wilcoxon rank-sum tests were used to compare continuous characteristics across these groups. Pearson correlations were calculated to determine the relationship between the number of drugs monitored and the various levels of FTE devoted to ASP-related activities. All statistical analyses were performed using SAS, version 9.3 (SAS), and P values less than .05 were considered statistically significant.

RESULTS

Individuals from 38 (91%) of 42 hospitals across the US responded (Figure 1). ASPs meeting our definition of continuously monitoring antimicrobials with dedicated FTEs were identified in 16 (42%) of the 38 hospitals. Hospitals with ASPs had more inpatient beds, patient-days, and patients undergoing solid-organ or bone marrow transplantations than did hospitals without ASPs (Table 1). Among the 22 hospitals without an ASP, 14 (65%) stated that they were in the process of developing a program. Hospitals without ASPs reported lack of funding (59%) and lack of personnel (41%) as the largest barriers to forming a program.

Of the 16 hospitals with ASPs, 13 (81%) were started after 2007, and no hospitals started an ASP between 2000 and 2007. The median number of total FTEs allotted to a program was 0.63 (range, 0.1–1.8 FTEs; Figure 2). Physician FTEs were

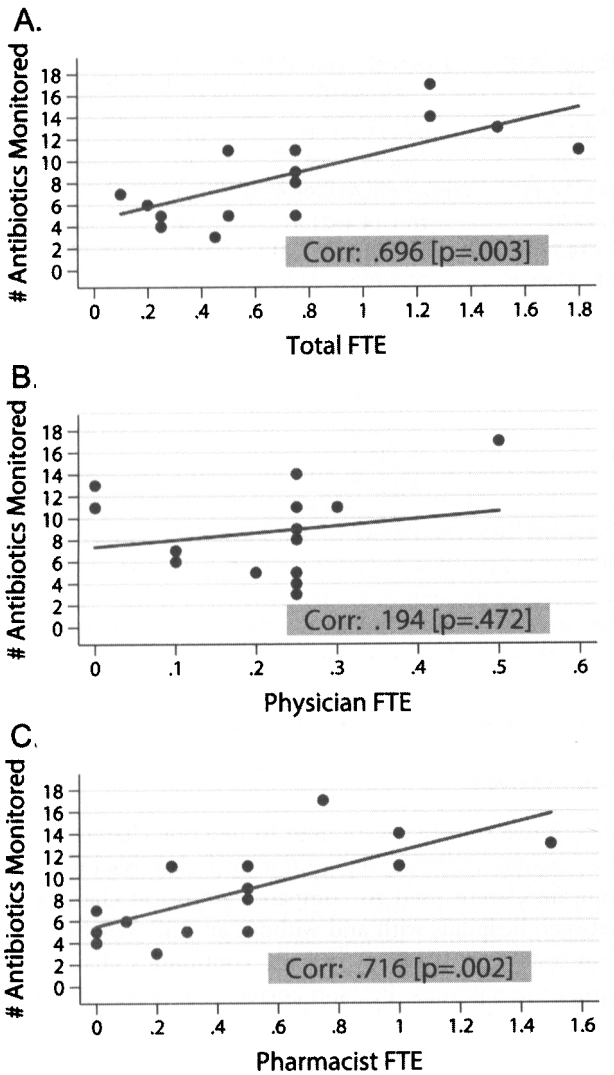

FIGURE 2. Relationships between type of full-time effort and number of monitored antibiotics for the 16 antimicrobial stewardship program (ASP) hospitals surveyed. *A*, Scatter plot of number of antimicrobials monitored versus total full-time equivalents (FTEs) dedicated to an ASP. *B*, Scatter plot of number of antimicrobials monitored versus physician FTEs dedicated to an ASP. *C*, Scatter plot of number of antimicrobials monitored versus pharmacist FTEs dedicated to an ASP.

reported in 14 (88%) of the 16 hospitals with ASPs, with a median FTE of 0.25 (range, 0.1–0.5 FTE), whereas 13 hospitals (81%) had dedicated pharmacist FTEs, with a median FTE of 0.5 (range, 0.1–1.5 FTE). Only 1 hospital (6%) with an ASP had data analyst support.

ASPs most often monitored linezolid, daptomycin, vancomycin, carbapenems, and fluoroquinolones (Figure 3). Conversely, several drug classes were monitored by 50% or fewer of the hospitals with ASPs; these drugs or drug classes included ampicillin-sulbactam, third-generation cephalosporins, and aminoglycosides. Only 1 hospital monitored the use of clindamycin. There was variation in the total number of antibiotics monitored by each hospital; 7 hospitals monitored 10 or more antimicrobials, whereas 9 hospitals monitored less than 10 antimicrobials. A positive correlation was observed between total FTEs ($r = 0.69$; $P = .003$) and number of pharmacist FTEs ($r = 0.71$; $P = .002$) with the number of antimicrobials monitored (Figure 2).

Strategies and electronic tools used to manage antimicrobials in hospitals with and without ASPs are listed in Table 2. Core antimicrobial stewardship strategies were used in 33 (87%) of the hospitals, most commonly prior approval/antimicrobial restriction. Most hospitals without a formal ASP also used these core strategies (18 [82%] of 22). Among hospitals without an ASP, 9 [41%] of 22 reported the use of prospective audit and feedback in some form; pharmacists performed this intervention in 6 hospitals, an ID physician in 1 hospital, and a pharmacist and ID physician in 2 hospitals. Among the supplemental strategies, clinical guidelines were available in 31 (82%) of 38 hospitals, although no difference was noted in guideline use by ASP status (77% vs 88%; $P = .675$). Management of bronchiolitis, pneumonia, and febrile infants were the most common guidelines present in these hospitals.

Among all hospitals, only 1 did not have an EHR. Furthermore, 31 (79%) were using CPOE. Computer surveillance software (eg, Theradoc, Sentri7, and Vigilanz) was used in 19 (49%) and was primarily used for infection control purposes. Only 5 hospitals (13%) used computerized decision support to influence antimicrobial use.

All respondents with ASPs and most respondents without ASPs (68%) reported monitoring outcomes relevant to antimicrobial use (Table 2). The most consistently monitored end points varied on the basis of the hospital's ASP status; ASP hospitals were more likely to monitor antibiotic use and costs than were hospitals without ASPs ($P = .02$). Hospitals were equally likely to monitor antibiotic resistance regardless of ASP status ($P = .74$).

DISCUSSION

Our study provides a detailed description of the current prevalence and characteristics of ASPs among freestanding children's hospitals in the United States. At the time of this survey (mid-2011), most (30 [79%] of 38) freestanding children's hospitals either had a formal ASP established or were in the process of developing a program. However, the approach, structure, and resources allocated to these programs varied across sites, and several hospitals without formal ASPs nonetheless performed core stewardship activities. Compared with hospitals without ASPs, hospitals with formal ASPs had more beds, higher patient volumes, and appeared to treat children with more medically complex cases. Characterizing the early adopters of ASPs and resources dedicated to ASPs may facilitate adoption by similar institutions. Additionally, these data will help future studies identify the components of pe-

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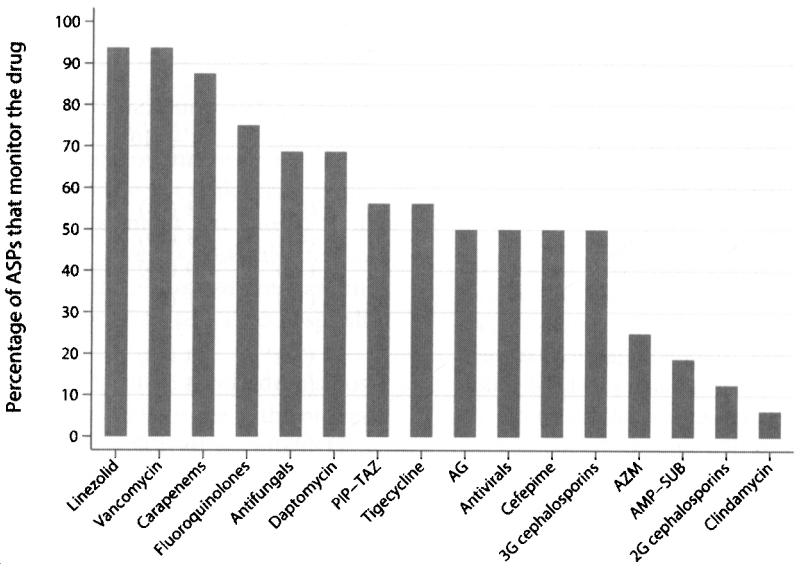

FIGURE 3. Proportion of antimicrobial stewardship programs (ASPs) monitoring the specified antimicrobials. 2G, second generation; 3G, third generation; AG, aminoglycoside; AMP-SUB, ampicillin-sulbactam; AZM, azithromycin; PIP-TAZ, piperacillin-tazobactam and ticarcillin-clavulanate.

diatric ASPs associated with the reduction in antimicrobial use and improved patient outcomes.

In light of the proven benefits of antimicrobial stewardship activities, the development of ASPs in tertiary care children's hospitals is encouraging. Furthermore, it appears that the most rapid uptake of ASPs occurred after 2007, after publication of IDSA guidelines outlining the design, implementation, and operation of such programs.[1] Although evidence emerged supporting the benefits of ASPs with respect to optimizing antimicrobial prescribing and reducing unnecessary costs, recognition of burgeoning antibiotic resistance occurred across the globe.[8-10] Therefore, the true impact of the publication of ASP guidelines on program formation is unclear. Also, because early adopters of ASPs were generally larger institutions with patients whose cases were more medically complex, these centers may have had the necessary components in place when the guidelines and related recommendations were published. We found that financial factors were the most important barriers to program development, despite cost savings being the most consistently demonstrated outcome associated with ASPs.[4,11,12] A better understanding of the barriers to program development as well as the strategies most effective in garnering support for ASPs (eg, formalized business plans) are important to make progress toward universal development of ASPs in pediatric settings.

There were significant differences in ASP structure across hospitals. Both the total number of FTEs dedicated to the program and the specific roles to which these FTEs were allocated varied widely. Although core personnel generally included infectious diseases physicians and clinical pharmacists, the number of total FTEs ranged more than tenfold across centers with formal ASPs. Only a single program supported a data analyst, which is a surprising finding given the critical importance of process and outcome data to monitor the impact of ASP activities both internally and across hospitals as well as to identify new targets for intervention. Additionally, the recent position paper from the IDSA, the Society of Hospital Epidemiology of America, and the Pediatric Infectious Diseases Society highlights the importance of using hospital-specific antimicrobial prescribing data to further enhance ASPs.[13]

Prior authorization and prospective audit and feedback were commonly used stewardship strategies, and programs with formal ASPs implemented both core strategies more frequently than did those without formal ASPs. We observed that institutions with a greater number of FTEs, especially for pharmacists, monitored more antimicrobial drugs. Pharmacist involvement in ASPs is associated with improved patient outcomes.[14] Additional investigation is required to determine whether more FTEs are associated with greater program effectiveness.

Many hospitals without formal ASPs were performing stewardship activities. For example, 9 hospitals without a formal ASP reported use of prospective audit and feedback. When incorporated into a formalized ASP, this strategy may require more resources in terms of time and personnel. It is essential to determine which strategies and activities perform best so that institutions with more limited resources can efficiently incorporate the most effective strategies. Expanded use of decision support systems may facilitate incorporation

TABLE 2. Comparison of Antimicrobial Management Strategies between Hospitals with and without Antimicrobial Stewardship Programs (ASPs)

Variable	No. (%) of respondents		
	Without ASP (n = 22)	With ASP (n = 16)	P
Main approach			
Prospective audit and feedback alone	2 (9)	2 (13)	.524
Formulary restriction alone	9 (41)	3 (19)	>.99
Both	7 (32)	10 (63)	.311
Neither specified	4 (18)	1 (6)	Reference
Other tools			
Clinical guideline	17 (77)	14 (88)	.675
Order form	4 (18)	5 (31)	.450
Technology			
EHR	21 (95)	16 (100)	.999
Computer surveillance	8 (36)	11 (69)	.099
CPOE	17 (77)	13 (81)	.999
Clinical decision support	7 (28)	5 (31)	.999
Outcomes monitored			
Any	15 (68)	16 (100)	.014
Antimicrobial use	7 (32)	12 (75)	.02
Antimicrobial costs	5 (23)	10 (63)	.02
Antimicrobial resistance	7 (32)	6 (38)	.742
Compliance with ASP recommendations	NA	12 (75)	NA
Rate of *Clostridium difficile* infection	16 (73)	6 (38)	.047

NOTE. CPOE, computer physician order entry; EHR, electronic health record; NA, not applicable.

of key stewardship activities in settings with fewer or no FTEs dedicated to an ASP.

The importance of enhancing our understanding of the most effective stewardship strategies is further illustrated by the substantial variability across institutions in structure and approaches used for their programs. This variability is to some extent inevitable, in part driven by local contextual factors but also by the absence of robust comparative effectiveness studies providing evidence of the "best" structure and strategy for antimicrobial stewardship. Among hospitals included in this study, significant variability in antimicrobial use has been demonstrated, even after controlling for hospital and patient factors.[15] Thus, identifying the specific components of an ASP with the most beneficial influence on relevant patient outcomes is crucial for future ASP development and in explaining the tremendous variability in antimicrobial use.

Broad-spectrum antibacterial agents, including linezolid, vancomycin, carbapenems, and fluoroquinolones, were monitored by most programs. However, these therapeutic agents comprise only 13% of total antimicrobial use among the PHIS hospitals. Presumably, these broad-spectrum agents are monitored either to contain costs, because these antibiotics are relatively expensive compared with narrow spectrum agents, or to limit the selection of resistant pathogens. However, some of the most commonly used broad-spectrum antimicrobials (eg, third- and fourth-generation cephalosporins) were monitored by only half of institutions with ASPs. Notably, clindamycin is monitored by only 1 hospital with an ASP, despite data among PHIS hospitals demonstrating a significant increase in use during the period 1999–2009 among patients with *S. aureus* infections.[16]

Monitoring outcomes is an important aspect of any stewardship program. Hospitals with an ASP were more likely to monitor antimicrobial use, which is not surprising. However, only 13 (31%) of 42 hospitals monitored antimicrobial resistance beyond their local antibiograms, and this was not impacted by the presence of an ASP. Interestingly, hospitals without an ASP were more likely to monitor *C. difficile* infection rates. Our survey instrument, however, did not assess the robustness of outcome monitoring, and it is unclear whether these differences affected antimicrobial use. Additional studies dedicated to assessing the impact of various ASP strategies on these outcomes are warranted.

This study has several limitations. First, the role or position of the survey respondent was not uniform across centers. Therefore, it is possible that the responding hospital epidemiologist, infectious diseases physician, or clinical pharmacist might not have been familiar with all of the hospital activities included in the survey. This variability may have had greater impact on responses from centers without formal ASPs. Second, because the specific elements defining a formal ASP have not been firmly established, our definition of an ASP might

have misclassified some hospitals as not having ASPs, which could result in bias toward the null in many of our comparisons. Indeed, many centers without ASPs (by the definition used in this study) performed antimicrobial stewardship activities. Third, although outcomes monitored by ASPs were assessed, the specifics of how this was performed and how it impacted the program were not evaluated. Finally, the generalizability of our findings might not extend to all children's hospitals; however, the surveyed hospitals are geographically diverse and account for 75% of the freestanding children's hospitals and 15%–20% of all pediatric hospitalizations in the United States.

In conclusion, the majority of freestanding children's hospitals have implemented ASPs since 2007 or are in the process of program development. Although single-center studies have indicated that ASPs are effective in improving antimicrobial prescribing, future studies that compare different structural features are needed to determine the most effective approaches and strategies for stewardship in pediatric settings.

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